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THE USE OF ISOTOPES IN SURGICAL RESEARCH

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THE rapidly widening horizon of medical research with radioactive and stable isotopes of the common biologically important elements has long since come to include the sphere of surgery. Indeed, surgeons were among the earliest of the clinical groups to employ these useful tools in the study of physiologic and biologic problems.

Such materials are now becoming widely available for surgical research in this country and in foreign countries; it is especially appropriate to review in brief some of the salient points of the history of this type of work, its biologic potentialities and a few of the practical problems facing the investigator. It is with this purpose in mind that the material presented herewith has been gathered together.

It is important to acknowledge at the outset that the author is not a physicist; he has had little contact with the recent physical marvels from betatron to Bikini. The thoughts expressed herein are based on a limited experience over a 7 year period with radioactive isotopes of bromine, chlorine, iodine, sodium, potassium, iron, phosphorus, and with deuterium. Although we must deny that research with isotopes is a field in itself any more than research with a colorimeter constitutes a field in itself, there are certain pertinent considerations which may help the investigator. It is our present purpose to outline some of these—though they may seem elementary to some, controversial to others. The fundamental physics of the materials and devices herein discussed are set forth in several standard works and no effort to review this material will be made in this paper (12, 21, 31, 36, 40, 43, 44, 56, 68).

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The period of cyclotron production of radioactive isotopes for biologic research (1939-1945) saw the initial exploration of this area by a small number of investigators. On the physical side, techniques of production, separation, and measurement of radioactive isotopes of most of the biologically important elements were developed. Biologically, the *in vivo* distribution of these substances was studied, permeability and rates of exchange were observed where possible, and in certain instances the incorporation of active atoms into the complex organic materials was investigated.

Many lessons about investigative technique were learned. Though the use of radioactive materials involves many physical problems, and though the physicists were responsible for the discovery, production, and separation of the isotopes, and their measurement, the medical application of these materials was soon found to be a biological or biochemical problem at heart—with physics only as handmaiden.

If one is to study bone physiology with Ca^{45}, it is important to know what, in general, is meant by a beta-ray energy of 0.25 Mev as this concerns the counter-window thickness,

or the preparation of samples with a constant coefficient of self-absorption; it is wise to be aware of the relation of half-life to working usefulness of the isotope mixture. If these considerations be physics, then they must be accepted as such and learned. But the intimate kinetics of the nuclear reaction involved, the gain or loss of a neutron, the factors involved in "capture cross-section," and similar matters are physical and technical problems whose details need not concern the medical investigator. In the sense of time spent, the less he knows about them the better. To use a photoelectric colorimeter, one need not study the physical basis of light transmission, absorption, and optical systems, as long as the essential limiting factors are understood and given their due respect.

This was the first lesson learned in the cyclotron period: though the application of isotopes to medical and biological research is in effect a collaboration between biochemist and physicist, it is the biologist who must point the way and name the destination.

The second lesson learned from the cyclotron was a corollary to the first and might be stated thus: "Isotopes do not solve problems." Isotopes plus intelligent biological conduct of the experiment and its ancillary concepts, techniques, and analyses are capable of giving more answers than the concepts, techniques, and analyses alone. The radioactive material and the Geiger-counter result do not provide solutions by themselves—it is their *biological context* which gives them meaning and significance. If this context is well planned and executed, the result is often of great importance; if not, the radioactivity might as well have been allowed to decay quietly behind its lead shielding.

Now, temporarily at least, the cyclotron is somewhat less important in the medical picture. That colorful and temperamental device is undergoing expansion and perfection at the hands of its progenitors, the physicists. Its unpredictable vicissitudes have been replaced by forms in quadruplicate and on-the-clock delivery of materials formerly obtained only with difficulty. The cyclotron has given way to the chain-reacting pile (1, 48, 64).

This new source of radioactive material for biological research has opened the way for investigators not situated in the established physical-biological centers; the pile makes these materials available to many rather than only a few of the country's surgical laboratories. Among the many newcomers to this field will be those who make the significant discoveries of the next decade; their ability to produce worth-while information will be a function of preliminary understanding of the biologic problems they seek to solve. The more who set out, the greater likelihood of a few reaching the goal—and therein lies the true importance of the pile: it mass-produces a precious scarcity item.

I. TYPES OF PROBLEMS

Although the types of biological research which may be carried out with radioactive isotopes are many, they tend to arrange themselves into several significant subheadings.

1. Permeability and membrane transfer. In the study of the penetration of ions or molecules from one area of the body fluids to another, isotopes make their greatest fundamental contribution to research. It is impossible to study certain types of membrane-permeability problems without tagged substances of some sort. Though one may place the red cell in plasma and carry out studies of the chemical constituents of the red cell and of the surrounding plasma, it is difficult to assess the permeability of the normal, healthy, red-cell membrane to its contained ions without the use of isotopes (6, 50). The essential function of the isotope in this type of study is to allow the investigator to place all the material he is tracing in one or the other compartment and still maintain the system in chemical equilibrium. As one contemplates a red cell in its plasma, it is apparent that there is potassium on both sides of the membrane. If the investigator alters the cell or its medium in such a way that the total chemical composition within the red cell changes by increasing its potassium content, it is of course clear that this potassium has come into the red cell from the surrounding plasma because there is no other source for it. But under stable equilibrium conditions such as those which obtain

in the body in the absence of disease, one has no way of knowing whether or not any of the potassium within the red cell can exchange with the potassium in the surrounding medium unless there can be placed in the plasma a form of potassium which is identifiable, once it gets into the red cell, as having come from the plasma. In such cell-permeability problems, tagged substances provide the only means of obtaining a satisfactory answer. Whether that membrane be the capillary, the lymphatic, the cell, the nucleus, or some special barrier such as the glomerulus or choroid plexus, and whether the tracer be an ion or a large protein molecule, isotopic techniques inform the investigator of the relationships between the two sides of the membrane in a fashion which cannot be gained in any other way.

2. *Tracing metabolic pathways.* Though we can dissect a whole animal and analyze its constituent organs chemically for an element, we have no way of knowing the previous position of the element as found in the various organs, nor its distance in point of time or metabolic pathway from its source, such as the gastrointestinal tract. By the use of a tagged element it is possible to give one radioactive dose to the organism and at varying periods after administration to analyze the animal and find the position in the various organs and body fluids of this single dose. When one has analyzed the whole organism some hours after a feeding containing a radioactive element, the distribution which one finds is presumably typical for the distribution of any similar amount of stable element administered the organism. The total dose given must be carefully considered in this type of work. The smaller the total gravimetric quantity of the element used (the more closely it approximates a true "tracer" dose) the more one may assume that its metabolism has been typical of the organism's handling of a single dose of that substance. If the radioactive material is given in a large dietary amount of isotopic mixture, then, of course, other problems such as toxicology and kidney function may be brought into play. By such studies of individual ions or elements much has been learned of the dietary metabolism of such substances as calcium, iron, iodine, and the physiologically important electrolytes. Now, with radioactive molecules of greater complexity becoming available, more of this type of metabolic-pathway mapping may be carried out, relative to the metabolism of complex organic materials.

3. *Utilization by specific organs.* As a refinement of the above investigation, it is possible by means of isotopes to study the utilization of elements or compounds by specific organs. An outstanding example of this historically is the utilization by the thyroid of iodine (32, 33). The physical and biological characteristics of iodine were in a sense a fortunate coincidence to the early workers in biology using radioactive isotopes. Certain radioactive isotopes of iodine are readily produced; their physical emanations adapt themselves well to ordinary measurement techniques; and the spectacular localization of nearly all of this element in one organ provided materials for tissue study which has yielded a mass of important information. Alteration of biological conditions either in the organism as a whole or in the tissue itself, studies in tissue culture, studies in health and disease, as well as methods of therapy, have grown from this work. Had the radioactive isotopes of calcium, sulfur, nitrogen, carbon, oxygen, and hydrogen been as readily applied to biological experiment as iodine has been, what a mass of work already would have been accomplished on other important metabolic problems!

The autoradiograph presents the most intimate picture of utilization of elements or compounds by specific tissues, and belongs in this category of observation. The autoradiograph is a record made on photographic emulsion by the beta radiation of isotopes previously administered to the animal or patient; by comparison with microscopic slides and suitable magnification, exact histochemical localization of isotopes may be obtained (3, 45, 46).

4. *External localization.* The concept of injecting a radioactive substance into an animal or a patient and then casting about over the living organism with a Geiger counter to find out where the element went, has gripped the imagination of investigators and public for many years. In the case of the thyroid the selective localization of the radio-iodine in

thyroid tissue, wherever that tissue is, has provided again, by coincidence, a ready application of such methods (33). Studies of the circulation by externally placed counters, using Na^{24}, have also been carried out (63). Here, however, the lack of selective localization makes interpretation much more difficult. Attempts to collimate the beam of radiation by suitable screening of the counter occasionally help, but such efforts nearly always interpose a greater distance between the radioactive source and the counting instrument in such a fashion that, by the law of inverse squares, intensity is sacrificed for point localization. Experience with radioactive dyes and their localization in abscesses demonstrated that at least in the case of radiobromine external localization could best be produced by a minimum of lead shielding and also a minimum of distance between the radioactive source and the counting instrument (52, 65). The inverse-square law is the investigator's best friend in this type of work; the intensity of counting rates using external counters on the intact organism is found to have a characteristic pattern for almost any element or compound used; departures from this pattern are the significant finding and these departures are readily demonstrated with an unscreened and closely placed counter if the normal distribution is well understood as a preliminary. Variations in thickness of the subcutaneous tissues and skin produce such differences in counting rates that quantitative relationships between dose and external measurement are difficult to establish except on an empirical basis.[1]

5. "Tagging" of complex compounds. The study of complex compounds appears to represent a principal future effort in isotope research. Attempts to label complex organic materials with radioactive isotopes go back to the earliest days of the cyclotron. Many physiologically important molecules which contain such elements as carbon, phosphorus, iodine, iron, or sulfur, and which were susceptible of synthesis, could be synthesized with the radioelement in place of its stable isotope (13, 47, 61, 62). It is apparent from casual consideration of this problem that for the tracing technique to be valid the element involved must be in "stable" linkage in the organic compound. If one uses sodium or lithium salts of a compound with the radioactivity on the cation, dissociation in solution separates the activity from the compound in question and subsequent counting rates are nonsignificant (72). Furthermore, certain compounds may be subjected to such rapid metabolic breakdown that the tagging element is rapidly divorced from its chemical partner, and subsequent physical analyses yield little information other than that concerning breakdown. In addition to tagging compounds which already contained the element made radioactive, compounds were tagged by the extrinsic linkage of radioactive substances such as bromine or iodine (23, 66). These compounds provided much interesting information but occasionally suffered from the fact that the radioactive halogen or other element attached to the organic molecule so changed its behavior that physiologic measurements were misleading as regards the behavior of the normal substances in the organism.

The work of Schoenheimer and his co-workers with heavy nitrogen and deuterium has pointed the way for the future of this field (59). Their work and the work of Conant and Hastings with carbon (7) demonstrated the fundamental importance of using tracers made from the biologically most important elements, those of carbon, hydrogen, oxygen, and nitrogen. By such techniques, paying careful attention to the precise chemical position of the tagging substance and the stability of the tagging linkage, the physiologic behavior of most of the important compounds of the body may be studied. Compounds which cannot be synthesized in the laboratory may be made radioactive by using natural syntheses carried out by the living organism. Such methods have already yielded much information on hemoglobin metabolism (using radioiron) (30) and on protein metabolism (using sulfur) (61, 62). There are other examples where living organisms or bacteria have been used as a synthetic partner in such researches. The present availability of C^{14} has an almost front-rank

[1] It should be mentioned in this connection that although gamma rays penetrate tissue to a far greater extent than beta radiation, their importance in external counting problems is not proportionally great because of the far lesser ionization produced per unit of path and, hence, the lesser counting efficiency in the measurement of gamma radiation.

importance in isotope research because of its use in the study of the more complex organic compounds.

6. Fluid space measurement. The measurement of volumes of body fluid available for the solution of an ion may be carried out by dissolving a tracer for that ion in the body fluid space in question, allowing mixing to occur, making appropriate corrections for excretion, and then studying the final dilution obtained. The tracers used for this type of work have classically not been radioactive. The use of bromine as a tracer for chlorine allowed Hastings to make many of his fundamental observations on the extracellular space (67). The use of the blue dye as a tracer for plasma protein has enabled investigators to make measurements of the plasma volume (15, 24, 28, 41). Other techniques involving the use of isotopic tracers have developed measurements of the extracellular space (using radiosodium or radiobromine) (39) and total body water (using deuterium) (50). By the use of the same fundamental calculation, the total quantity of other elements in the body may be determined. These methods will be dealt with in greater detail below.

7. Therapy with radioactive isotopes. This is an application of radioactive isotopes dependent upon selective localization in pathologic tissues. In a sense, this occupies a separate position from the strictly investigative use of the isotopes and as such will not be dealt with further in this article.

II. ARRANGEMENT OF PROJECTS

It is wise, in setting up a research project employing radioactive isotopes, to follow certain general principles. The first of these has to do with physical collaboration.

1. Collaboration of physicists. At the present time, when pile-produced isotopes are used, the collaboration of a department of physics for the production of isotopes is no longer as essential as it formerly was. The co-operation of persons trained in radiochemistry is of vital importance if the investigator does not have at hand either the chemical or physical techniques required in the separation or preparation of isotopes for biological utilization. The most important aspect of this at the present time has to do with safety precautions; special equipment is required in the handling, purification, separation, and dilution of isotopes which are received from the Atomic Energy Commission, especially if these are shipped in the dry state. Commercial enterprises making such services available are coming into being at the present time and will remove a very real burden from the physicists.

For detection and measurement of isotopes in the tissues or body fluids which represent the end-points of the investigation, the help of the physicist is often required in the setting up or designing of apparatus. It is a mistake, however, to set up a research project with a detached physicist performing the sample measurements in a laboratory far removed from the biological aspects of the experiment. Under these circumstances the accurate correlation of physical and biological measurements which is so necessary to success is difficult. Furthermore, this type of project, in which the physicist is used simply as a technician to make or supervise the end-point readings, places the physicist and his laboratory in an unsatisfactory position and constitutes "research by committee," a notoriously inefficient way of operating. If the isotopes used emit beta-rays with energies sufficient to be measured on ordinary counting apparatus, it is advisable for any research project to be organized in such a fashion that end-point measurements may be made in the laboratory in which the biological experiments are carried out. The services and support of a well-qualified physicist to help solve problems which come up relative to radioactive contaminants, double isotope experiments, or measurements of unusual or difficult substances such as gases or weak radiation, should be available. Such a research project will be most successful if the physicist plays the rôle of consultant and is not relied upon too heavily for isotope preparation, sample measurements, or biologic interpretation.

2. Cost of equipment. The cost of research with isotopes is still greater than that of many other types of biological investigation. The necessary physical equipment at the present time costs approximately five hundred to one

thousand dollars, if special problems do not arise relative to weak beta-ray energies or other special counting problems such as C^{14}. If the investigator is able to tinker with electronic devices, he may be capable of setting up his detection apparatus with less capital outlay, using equipment which is less complicated.

The cost of isotopes appears to be very small in the catalogue issued by the Atomic Energy Commission. If the isotope has a long enough half-life, so that it may be shipped by rail, the only cost which need be added to the catalogue list price of the Oak Ridge isotope is the cost of handling and shipment, which will not total much more than twenty-five dollars for each shipment. To this, however, must in many cases be added two other types of charges. One is for air freight, a charge necessary if the isotope has a half-life of less than a week. This charge runs in the neighborhood of fifty to one hundred dollars for the distances ordinarily encountered in this country, using the lead shield containers standardized by the Atomic Energy Commission. The second additional charge which may arise has to do with the separation and handling of the isotope. If high activities of strong beta-ray energy are received, the investigator may wish to pay someone else to handle the initial preparation and dilution rather than to set up the equipment in his laboratory necessary for a "hot" shipment. This may add another twenty or thirty dollars to the cost of each unit. While such services may be expensive, they must be counted against the necessary cost of setting up facilities for the storage and handling of such dangerous activities in the ordinary biological or hospital laboratory.

In general, a laboratory which has not previously employed isotopes may well have to set aside from twenty-five hundred to five thousand dollars for the expenses of embarking on this type of research. There are less expensive ways of employing isotopes to cast light on a biological problem, one being by the use of an electroscope for sample measurements, and the other by sharing a bombardment with other laboratories. Both of these methods of employing isotopes will be discussed later in this article.

III. HANDLING THE RADIOACTIVE MATERIAL

1. Safety measures. Safety precautions which may be taken during the handling of radioactive materials divide themselves into two headings. One of these may be called "precaution against injury," and the other may be called "precaution against liability" (17).

The separation of precautions into these two categories may appear cynical; one might be of the opinion that precaution against liability would, of course, involve precaution against actual injury. While not enough experience has been gained to permit any final answer to this problem, it seems reasonable to assume that suit may be brought against laboratories or laboratory directors for imagined injury from radioactive material, and that a verdict for the plaintiff might be granted if it were not established that reasonable precautions were being taken. Under the circumstances of biological investigation with radioactive isotopes in the usual hospital environment, such "reasonable precautions" include the storage and placing of high activities away from personnel, the wearing of badges or other radiation recording devices, and the avoidance of too frequent exposure to high activities.[1]

Therefore, under the other heading of actual "precaution against injury" should come the more fundamental considerations having to do with education of personnel. Individuals working with these materials must be shown, by actual examples employing a Geiger counter, how time and distance are the two greatest safety devices known. If the technician or research assistant can avoid exposure to activities for any more than the absolute minimum length of time, and can have these exposures at maximum distance, he will have done more for himself than lead gloves, photographic film, or blood counts can possibly accomplish. This statement, of course, does not apply to those working near cyclotrons or potent neutron sources such as the pile. We refer entirely to the circumstances of ordinary biological investigation in medical school or hospital.

[1]The reader is referred to circular B-1 ("General Rules and Procedures Concerning Radioactive Hazards") and B-2 ("Health Protection in Handling Radioisotopes") issued by the Isotopes Branch, United States Atomic Energy Commission, P.O. Box E, Oak Ridge, Tennessee.

In our opinion, the most vulnerable point in the technique of handling radioactive isotopes in medical investigation is the fingertip. There is little evidence that the amounts of radiation involved even with the use of isotopes emitting energetic beta and gamma rays will do damage to bone marrow or gonadal function *when only tracer amounts are involved*. However, fingertip contamination or even fingertip exposure might lead to serious subsequent injury. One should bear in mind that if the fingertip is 2 centimeters away from the flask and the sternum is 80 centimeters away, the fingertip is receiving 1,600 times as much radiation as the sternum per unit of flat surface. Furthermore, the fingertip, unlike the sternum or the region of the gonads, may be contaminated by liquid containing fairly high activities—as is found in a freshly diluted specimen of pile-produced activity prior to injection into the animal or patient. Such fingertip contamination is notoriously difficult or impossible to remove. Anyone who has had experience in this area knows the consternation encountered when, after scrubbing one's hands for 10 minutes, they are placed under a Geiger counter and an intense discharge of counts is produced. This dramatically demonstrates the fact that in working with radioactive materials one is dealing with atoms, and that they cannot all be removed even with a scrubbrush.

Protection of fingertips can be aided by the use of rubber gloves when high activities are handled. The rubber has no shielding value, but it prevents actual liquid contamination of finger creases and fingernails; the use on the fingers of rings containing photographic film is still in an experimental stage and may add a useful precaution. However, in the last analysis we come back to our old friends, education, time, and distance.

If our present knowledge of exposure hazards and safety factors were complete, it would be possible to list the late effects in human beings of the subclinical radiation dosages encountered in biologic research. That knowledge is not complete; and excessive, possibly unnecessary, precautions are justified. One need only recall the damage and suffering which resulted from early and seemingly cautious use of the roentgen-ray to understand the necessity for excessive caution necessary in this field.

Precaution against injury should be uppermost in the investigator's mind—yet he should remember that the carrying out of certain standard forms of safety measures may also act as a precaution against liability. The storage of high-activity samples behind adequate lead shielding, checked by a monitor device (either counter or electroscope) in all six planes of the storage cube, is an essential precaution. It is wise to place the storage unit in such a way that no personnel are steadily exposed to it though many may be intermittently exposed to infinitesimal doses by passing the neighborhood of the storage area.

2. Insurance. Closely related to the subject of precaution against liability, is insurance. Insurance may be divided into those policies which protect the investigator and his institution against justified claims arising from injury to qualified personnel while working under standard safety measures, and on the other hand those policies which are written to protect the investigator or institution from claims arising from personnel not qualified or not associated with the research who have suffered psychic trauma or imagined physical injury as result of proximity to the radiation source, either during shipment, storage, or use.[1] A third type of policy should be mentioned—that which covers liability for real or imagined injury to patients who have received injections of radioactive materials either for study or treatment.

The use of radioactive materials is not widespread enough at present to fall into "standard practice," and the range of liability is as yet undefined.

Of these three types of policy, the first would appear to be the most essential. Late radiation injury might not manifest itself for years, and workers who handle activities of any magnitude should be protected against the

[1]An example of the expense of such "public liability" policies may be gained from the fact that a premium of $150 per shipment has been quoted for a policy with limits of $100,000 per individual payment and $300,000 per total collection for any one suit. Property damage of $100,000 per accident was included. This quotation was for K^{42} in air transit. This premium may go up to $250 if the consignee accepts full responsibility from the shipping point.

TABLE I.*—RADIOACTIVE ISOTOPES OF COMMON BIOLOGICALLY IMPORTANT ELEMENTS ARRANGED ACCORDING TO HALF-LIFE

Element	Isotope	Half-life	
Oxygen	O^{15}	2.10 minutes	Group 1. Half-life less than 1.0 hour; time relationships become the conditioning factor in biological experimentation.
Nitrogen	N^{13}	9.93 minutes	
Magnesium	Mg^{27}	10.2 minutes	
Carbon	C^{11}	20.5 minutes	
Chlorine	Cl^{38}	37.0 minutes	
Potassium	K^{42}	12.4 hours	Group 2. Half-life from 1.0 to 36.0 hours; time relationships preclude "chronic" experiments; satisfactory for most "acute" experiments.
Iodine	I^{130}	12.6 hours	
Sodium	Na^{24}	14.8 hours	
Bromine	Br^{82}	34.0 hours	
Iodine	I^{131}	8.0 days	Group 3. Half-life 36 hours to 21 days. Satisfactory for wide biologic, synthetic and dietary experimentation.
Phosphorus	P^{32}	14.3 days	
Iron	Fe^{59}	44 days	Group 4. Half-life over 21 days. Biological potentialities essentially unlimited as to time.
Sulfur	S^{35}	88 days	
Calcium	Ca^{45}	180 days	
Zinc	Zn^{65}	250 days	
Sodium	Na^{22}	3 years	
Iron	Fe^{55}	5 years	
Hydrogen	H^{3}	31 years	
Carbon	C^{14}	5,100 years	

*This and the subsequent table are based on data to be found in bibliographic references (12, 44, 56, 68). In addition, the author is indebted to Professor John W. Irvine, Jr., of the Massachusetts Institute of Technology, for revisions which bring the data into accordance with the most recent available physical observations.

costs of occupational illness.[1] The second type of policy—that written to cover public liability from suits arising from transport accidents and subsequent imagined injury, or to cover judgments for the plaintiff in suits brought by lay people who blame illness (miscarriage, sterility, cancer) on established previous exposure—is so expensive as to be almost prohibitive. Any large, modern hospital employing the techniques of surgery, x-ray, and drug therapy, and acknowledging the hazards of these, runs such risks daily without the expense of blanket liability policies.

The third type of policy, essentially a form of malpractice insurance, should be adapted to the uses and practices of the particular investigator involved. Anyone treating nonmalignant disease with high activities (thyrotoxicosis, polycythemia vera) should seriously consider this type of insurance much as an x-ray department insures itself.

[1]As nearly as can be determined, the occupational hazard comes under the scope of voluntary or compulsory Workmen's Compensation Insurance in most states.

3. Sharing isotopes. In many instances one irradiation unit from the Atomic Energy Commission contains more material than can be used by a single research. Such excess material may often be made available to others who will share its cost. Not infrequently pile-produced activities are of lower specific activity than isotopes formed in a cyclotron by deuteron bombardment (Example: Na^{24}) and the amount of activity present is not as great as one might expect from the weight of isotope mixture. Before any commitments are made for sharing, it is well to view such considerations realistically.

Each university center where biologic and medical research is in progress could well maintain an "isotope registry" where dates and amounts of material expected are listed. In this way a maximum utilization of material would be achieved with minimum waste; sharing opportunities would not be overlooked. Before sharing materials obtained from the Atomic Energy Commission, one should pay due respect to the regulations covering "clearance" of each worker sharing the radioactive material.

IV. EXPERIMENTAL DETAILS

1. Preparation for administration. Whether the radioactive material is to be traced in its passage from a segment of body water into a specific compartment, tissue, or compound, or is to be followed from a specific site outward, the dose depends fundamentally on the maximum dilution and the time to elapse before measurement. In working with an ion, one may estimate this maximum dilution from the area of body water available for its solution. For the extracellular ions (Examples: Na, Cl, Br) about 20 per cent of the organism's body weight will represent the average maximum dilution and, hence, determine the probable maximum radioactive strength after equilibrium has been attained, whether the final measurements be carried out in plasma, urine, or other body fluids. Intracellular ions (K, Mg, SO_4, PO_4) are diluted in total body water with a lopsided distribution toward the cell,

leaving only residual amounts in plasma, though equilibrium is much more slowly attained. Isotopes injected as a part of organic compounds will, of course, follow the distribution of that compound or its breakdown products. Frequently considerable trial and error are necessary to establish the minimum dose which will yield satisfactory readings hours or days later when the measurements are made. In animal work the use of a minimum allowable dose is less important than in human studies, though in either case the use of unnecessarily large radioactive doses constitutes a hazard to those injecting the original, more-concentrated solution, and may in certain cases (Example: iodine) actually alter the manner of utilization by direct radiation effect on the cells which take it up (58). In studies made with human beings the importance of avoiding overdosage in tracer studies is self-evident.

Time relationships as they affect dosage naturally depend on the relation of experiment-duration to half-life of the material (Table I). The longer-lived isotopes such as Fe^{59}, P^{32}, Ca^{45}, S^{35}, and C^{14} (Groups 3 and 4, Table I) present little problem. Those in Group 2 (Na^{24}, Br^{82}, K^{42}) present a real problem, since inordinately high initial dosages may be necessary if the experiment is to last several half-lives before end-point measurements are made. With this group of isotopes, very careful timing and dose calculation must be carried out to avoid high dosage and radiation effects on man or animal or, on the other hand, a failure from readings too close to background. In the short-lived group (Cl^{38}, C^{11}) time looms larger than anything else in planning the dosage and conduct of the experiment. In both the latter groups of isotopes, measurement techniques which concentrate the element in question or which employ crude extracts of large amounts of body fluid or tissue may help the investigator over the hurdle of short half-life, though when such methods are used careful account must be taken of self-absorption.

2. Measurement. Just as the biologically important isotopes may be grouped according to their half-lives, so may they be grouped according to the energy of their beta rays and, hence, the ease and technique with which they may be measured (Table II).[1] The "strong" group includes Na^{24}, K^{42}, Cl^{38}, P^{32}, I^{131}. These are easily quantitated with standard equipment readily obtainable. The "middle" group, S^{35}, Ca^{45}, Fe^{59}, require special attention to self-absorption, counter or electroscope-window thickness and methods of concentration, purification, precipitation, or electroplating. The "weak" group, H^3, Fe^{55}, present such problems in measurement that techniques are still in process of development, and it is possible that the most practical and reliable have not yet

TABLE II.—RADIOACTIVE ISOTOPES OF COMMON BIOLOGICALLY IMPORTANT ELEMENTS ARRANGED ACCORDING TO ENERGY OF EMITTED PARTICLES

Element	Isotope	Particle energy in Mev (Max)	Gamma radiation Mev (Max)	
Hydrogen	H^3	0.015 e^-		Group 1. Radiation energy less than 0.1 Mev; technology of detection complex and still developmental.
Iron	Fe^{55}	0.009 Mev X-ray		
Carbon	C^{14}	0.145 e^-		Group 2. Radiation energy from 0.1 Mev to 0.5 Mev; technology of detection now available but close attention must be paid to problems of self-absorption, and special equipment may be necessary for accurate measurement.
Sulfur	S^{35}	0.170 e^-		
Calcium	Ca^{45}	0.250 e^-		
Zinc	Zn^{65}	(.400 e^+)†	1.14	
Iron	Fe^{59}	0.460 e^-	1.3	
Bromine	Br^{82}	0.465 e^-	1.35	
Sodium	Na^{22}*	0.58 e^+	1.30	Group 3. Radiation energy over 0.5 Mev; may be measured with ease on standard commercial equipment; hazards of handling "tracer" quantities greater than in Groups 1 and 2.
Iodine	I^{131}	0.69 e^-	0.37	
Iodine	I^{130}*	1.03 e^-	0.54	
Nitrogen	N^{13}	1.20 e^+	0.28	
Sodium	Na^{24}	1.40 e^-	3.73	
Phosphorus	P^{32}	1.69 e^-		
Oxygen	O^{15}	1.70 e^+		
Magnesium	Mg^{27}	1.80 e^-	1.02	
Carbon	C^{11}	3.40 e^+		
Potassium	K^{42}	3.58 e^-	1.51	
Chlorine	Cl^{38}	5.00 e^-	2.15	

*Produced only on cyclotron at the present time.
†Particle emission in small fraction of disintegrations and, therefore, of little significance in measurement.

[1] It will be observed in Tables I and II that many of the elements of weakest radiation have the longer half-lives; as a general rule half life and particle energy are inversely proportional. There are certain outstanding exceptions such as oxygen (O^{15}) and magnesium (Mg^{27}).

been devised. Although C^{14} is placed in the "middle" group, the many types of physical apparatus in process of investigation for its measurement are still in a developmental phase and much technical advance in this important field may be expected in the next few years.

3. *Equipment.* At the present time a large number of different counters and scaling circuits are coming on the market, and comparatively little attention is paid to the simplest and least expensive radioactivity-measuring device of them all—the quartz fiber electroscope. This device may be used for virtually any experiment employing the "strong" group of isotopes; and even the "middle" group may be measured in this fashion, special instruments such as those made with a lacquer window being used, or techniques such as placing the sample within the instrument itself (60). Any laboratory equipped with these instruments will make instruction in isotope technique available to many students at little expense; there are no complicated electronics between the observer and the radiation he is measuring. An electroscope provides the beginner with many useful lessons in the problems of radiation detection and measurement; he must think for himself without the help of a vacuum tube.

The faults of the electroscope are to be found in its complete lack of automaticity (as the instrument is commonly employed) and the very time-consuming nature of measurements carried out on samples near the background rate of discharge of the instrument.

Counters vary in their precise anatomy and in the relationship of the sample to the counting element. For the "strong" and "middle" group of isotopes a simple end-window or side-window counter of rugged constitution and good electrical characteristics should be selected. As counters wear out, or may be broken or contaminated, it is well to choose one which can readily be replaced (so that the "standard geometry" of the measuring arrangements will not have to be changed in the event of breakdown) and to keep an extra one or two on hand.

The scaling circuits now available vary chiefly in price and automaticity. The price and automaticity increase in linear proportion to each other. By "automaticity" is meant the property of automatically stopping the instrument after a predetermined number of counts or, in some cases, making a continuous written record of the sample strength. A self-operating sample changer has been devised as the ultimate in automaticity (55). Such refinements should be scrupulously avoided by anyone seeking to start out in this field by making the sample measurements in his own laboratory.

The same instrument which carries the scaling circuits also feeds the high voltage into the counting element, and it is well therefore to employ one which has an accurate voltage meter so that the counter plateau may be accurately measured and the voltage maintained constant.

As a final practical consideration, it is well to remember that even now these electronic devices are prone to sudden collapse or complete prostration. When such occurs in the middle of a critical experiment, it may be extremely disquieting. The best precautions against such an eventuality are: to run the counter through a test of linearity and the scaler through a test of accuracy prior to each experiment; to use a scaling circuit which can be repaired nearby; and, last but not least, to keep an electroscope on hand.

3. *Preparation of samples—standards.* One would not use a colorimeter by placing the unknowns in a different physical relationship to the light source and photo cell each time a measurement is made. The space-relationships are an integral part of the reproducibility of the method. The same applies to radioactivity measurements: the samples must all be similarly prepared and placed in an identical relationship to the counting element for the results to have meaning. This concept goes under the title of "standard geometry." Its importance is clear and the point will not be labored here.

The matter of absolute standards is a more mooted question. Consider for a moment a fleck of NaCl under a counter, an infinitesimal fraction of whose Na atoms are Na^{24} rather than Na^{23}. Each time one of these undergoes decay it emits radiation. Such an electron may

go up, down, or sideways; it may never reach the counter window because of absorption in the universe of Na^{23} around it, or because it never started out with enough energy to get to the counter. It may be stopped in the counter window; or, as a final insult, it may pass through the counter so soon after its immediate predecessor that the counter itself has not recovered from the previous discharge in time to register its passage. It is, therefore, clear that all the electrons emitted by the Na^{24} do not cause a pulse to pass through the scaling circuit. When one considers that the absolute units of radiation intensity, the curie and the rutherford, are based on rate of disintegration, it becomes clear that accurate quantitation of radioactive isotopes involves a measurement of the absolute disintegration rate of that material in terms of "disintegrations per unit time." In dealing with ordinary counting equipment and under the geometrical conditions ordinarily employed, this problem is one to confound the biologist and give pause even to the physicist.

A curie is defined as the quantity of radon in radioactive equilibrium with 1 gram of radium, and involves a disintegration rate of about $3.67 \pm 0.03 \times 10^{10}$ disintegrating atoms per second per gram of radium. This unit should properly not be applied to radioactive substances outside the radium family.[1] The rutherford is defined as that amount of any radioactive isotope which disintegrates at the rate of 10^6 disintegrations per second. Complicated physical techniques are required to measure the absolute disintegration rate of Na^{24}. However, by the use of suitable standards calibrated with samples of known radioactive strength, one may approximate for purposes of rough estimation just what a microcurie, or a millirutherford, of Na^{24} will yield on one's own instrument in terms of counts per minute. The only importance which attaches to this has to do with radiation hazards. Successful biologic experiments may be carried through without any reference to absolute standards. Results may be expressed in terms of the injected dose, or counting rate, or in "units" relative to uranium or other arbitrary standards, or in any way which is clear and unequivocal. But it is important for the safety of both workers and subjects to know to a first approximation the absolute disintegration rate of the starting material, for only in this way can the investigator relate his safety precautions to the experience of others.[2] This knowledge is probably easiest

[1] The reader is referred to the much fuller discussion in the report: "Radioactivity Units & Standards," prepared by Professor Robley D. Evans, of the Massachusetts Institute of Technology, for the National Research Council, Division of Physical Sciences, Committee on Radioactivity, Subcommittee on Units, April 15, 1947.

[2] Calculation of the roentgen equivalence of systemically administered radioactive isotopes involves many pitfalls. The extent of tissue dilution, the phase volume of body water in which the isotope is diluted, and specific tissue affinity are biologic variables which must be taken into account. The physical aspects of converting tissue dosage from beta rays into roentgens (units of radiation based on air ionization), are complex; in many instances only an approximation can be calculated for this conversion.

Two simple formulas have been derived by Prof. Robley D. Evans of The Massachusetts Institute of Technology, which are quite useful in this connection. The first formula is an expression whereby one may calculate the daily dosage rate in roentgens per day (R), derived from an isotope which achieves an average tissue concentration (C) in millicuries per kilogram, and possessing an average particle-energy (E_{av}) measured in MEV:

$$R = 60CE_{av} \qquad (1)$$

It should be emphasized that R is a *maximal* value; the formula is applicable when the isotope is dispersed through a mass of tissue large enough so that the mean beta ray path falls within the tissue: surface is small compared to mass. For simple beta-ray spectra the average particle energy may be taken as $\frac{E_{max}}{3}$. When a gamma ray is also involved, the roentgen equivalence is increased by 10–20 per cent. This formula is most useful in dealing with long half-lived materials.

When a short half-life isotope is involved, the total dose is a more important calculation than the daily dose. Here the following formula applies:

$$D = 1.44\,RT \qquad (2)$$

where D is the total dose in roentgens, R the initial daily dose-rate arrived at by formula (1) and T the half-period in days.

An example of this calculation may be illustrative. Suppose an 80 kgm. man is given 0.6 MC of K^{42}. The isotope may be considered as diluted in all of body water (60 liters). Then,

$$R = (60C\frac{E_{max}}{3})1.2$$

$$R = 60 \times 0.01 \times \frac{3.58}{3} \times 1.2$$

$R = 0.857$ roentgens per day (initial dosage rate).

The factor ($\times 1.2$) is the correction for the presence of a gamma ray. Since K^{42} is a short-lived isotope (12.4 hours), the radiation delivered to tissue by the end of the first day is in the order of ½ that being delivered at the outset, so the half-life correction should be introduced, and the total dosage calculated:

$D = 1.44\,RT$
$D = 1.44 \times 0.857 \times 0.5$
$D = 0.62$ roentgens total dose.

This first approximation of the radiation dosage to which the patient has been subjected for study, should be considered with the fact that the generally regarded safe limit is 0.6 roentgens per week. Thus the K^{42} study could be repeated at weekly intervals indefinitely and fall within this margin of safety. Ordinary x-ray exposures involve total radiation of 3–5 r for a chest fluoroscopy and film, 60–80 r for a gastrointestinal series.

These formulas are discussed more fully in the article by Professor Evans entitled "Tissue Dosage in Radio-Isotope Therapy," *Am. J. Roentg.*, December, 1947. The formulas were presented at the 1946 meeting of the American Roentgen Ray Society, Symposium on Isotopes. The reader is also referred to the calculations described by W. E. Cohn in the Manhattan District Declassified Reports, 1946, 95: July 24.

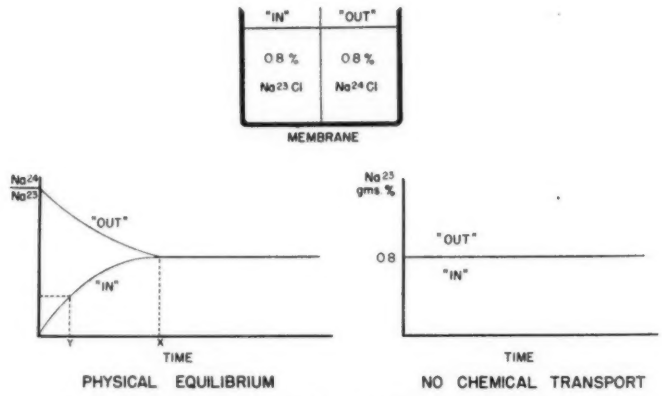

Fig. 1. Diagrammatic representation of a chemical situation in which physical (isotopic) equilibrium takes place without net chemical transport (i.e. without alteration in chemical concentration or distribution). The permeable membrane divides a beaker (above) into two parts, each of which contains physiological saline solution. To one portion ("Out") has been added a tracer amount of radiosodium (Na^{24}). The symbol $Na^{23}Cl$ denotes sodium chloride of the naturally occurring isotopic mixture; $Na^{24}Cl$ denotes sodium chloride containing a minute amount of radiosodium of mass 24.

Below, on the left, are shown the specific activity curves which denote the physical events which ensue in the face of such a situation. Physical equilibrium (unity of specific activity ratios) is attained as a function of time. On the right is shown the result of chemical analyses, which demonstrate no net chemical transport or alteration in concentration despite the active physical changes demonstrated by radioactivity measurements.

gained either by the use of uranium standards available from the United States Bureau of Standards, or by frequent comparison of standard samples with readings on instruments which have been calibrated in absolute units.

V. INTERPRETATION OF RESULTS

1. Specific activity. If one were to inject radiosodium into an organism prior to some trauma—such as a burn or surgical operation—wait 24 hours, and then do radioactivity measurements on all the tissues and body fluids, the investigator would be using his Geiger counter to do his chemistry for him; he would find out little by his measurements of beta-ray emission that he could not discover with a chemical determination.

During the hours which have elapsed between the injection and measurement, this Na^{24} has reached equilibrium with nearly all the Na^{23} in the body; each "unit" of radiosodium represents an underlying mass of stable sodium with which it has become mixed, and the relationship between various organs and tissues relative to sodium content are the same as their radiosodium content.

The relation of the radioactivity to the total sodium, rather than the radioactivity *per se*, constitutes the significant measurement. If the trauma has altered sodium distribution or the permeability of cells to sodium, such alterations will be demonstrated much more readily by this ratio of radioactive sodium to stable sodium than by the radioactive measurements alone, although activity measurements carried out before equilibrium has had time to occur may give a hint as to permeability changes. This important ratio is called the "specific radioactivity" and may be expressed as "rutherfords per gram," or "units per milliequivalent," or any other convenient expression of active-stable ratio. Under conditions of equilibrium the specific activity ratio will be the same wherever complete exchange has occurred; departures from unity in these specific activity ratios, in the case of sodium mentioned above, would indi-

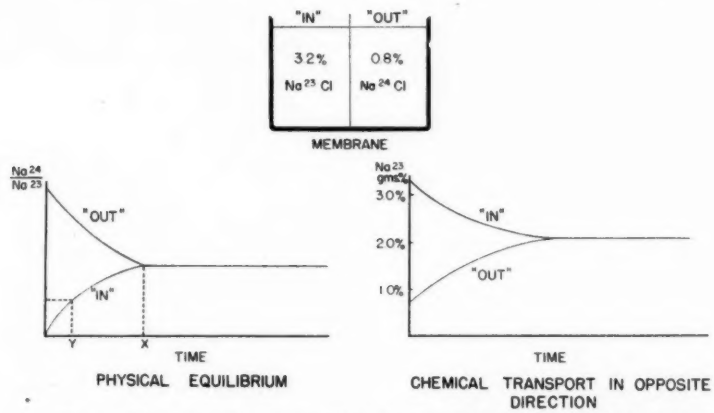

Fig. 2. Diagrammatic representation of a chemical situation in which physical (isotopic) equilibrium takes place despite net chemical transport in the opposite direction. Symbols and arrangements are as in Figure 1, except that the "In" compartment contains four times normal saline (3.2%) which produces an osmotic readjustment resulting in the net transport of sodium and chloride ions from "In" to "Out" before chemical equilibrium is re-established.

The addition of Na^{24} to the "Out" compartment produces a movement of radioactive ions from "Out" to "In," exactly as in Figure 1.

It is clear that the radioactive data alone, in such a situation, might be most misleading as to the true nature of the chemical process taking place.

cate differences in permeability to sodium, the presence of "bound" sodium which is not exchangeable, or failure to achieve equilibrium in the time elapsed.

Much radioactivity research with ions has suffered from a lack of concomitant chemical analyses and, hence, an absence of specific activity data. Even in work with more complex organic compounds, calculation of the specific activity will often reveal interpretative data not available from either physical or chemical analyses alone (10).

2. *Physical equilibrium vs. chemical transport.* If one were to make a gastric pouch and place therein a quantity of radioactive chloride, sodium, or even deuterium, the isotope would be seen to disappear from the pouch (4, 8, 9, 19). It would appear that the ion in question were being absorbed from the pouch. It was placed there, and now it is there no longer—surely the cells are actively absorbing the substance in question.

Such is not necessarily the case. Even if the gastric mucosa were actively secreting HCl at the moment, the Cl^{38} would still diminish both in total amount, concentration, and specific activity. The fact is that the Geiger counter and the cyclotron have put into our hands a means of detecting atomic quantities and we must no longer think in milligram terms when dealing with these unmeasurable weights.[1]

It is a fundamental assumption of all research with isotopes that the living cell, just as the passive membrane, cannot distinguish between isotopes of the same element. There appear to be a few interesting exceptions to this (Examples: H, D, H^3,—or I^{131} in high concentration, 40); but as a fundamental assumption it is sound. Therefore, as mixing of atoms occurs, a state of equilibrium develops in which unstable atoms are mixed with the same number of stable atoms in all parts of the system. The simplest example of this phenomenon is a unicameral solution of ions free of all externally induced motion—an absolutely still beaker of KCl for example. This

[1]In the most concentrated radioactive mixtures ordinarily available, only one-millionth or less of the atoms are unstable and capable of emitting radiation on stabilization. Only in the new "carrier-free" products of nuclear fission have "pure" radioactive preparations of the man-made isotopes been produced; and even here, if half-life is short and decay yields stable isotopes of the same element, radioactive purity will rapidly give way to diminishing specific activity. Long-lived carbon, C^{14}, as obtained from the Atomic Energy Commission contains about 3 per cent active atoms.

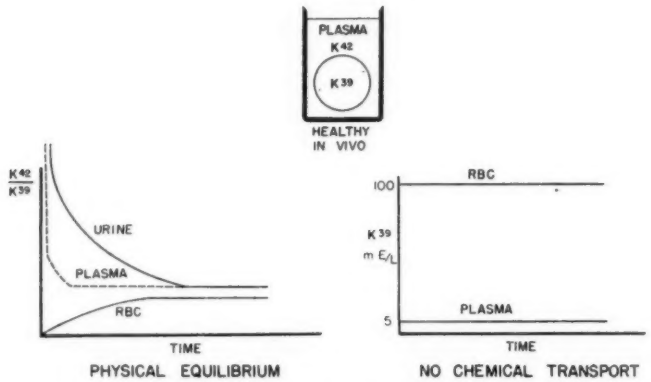

Fig. 3. Diagrammatic representation of a biological situation analogous to that shown in Figure 1. Although chemical equilibrium (stability) between potassium in the red cell and plasma is maintained by the peculiar properties of the viable erythrocyte, a physical redistribution occurs following the addition of K^{42} to the plasma by intravenous injection. Such an injection upsets the proportional distribution of isotopes and, as a result of the permeability of the red cell membrane to potassium, equilibrium is reestablished slowly; the nature of the curves suggests that a fraction of the potassium in the red cell is only slowly exchangeable with plasma potassium.[1] Analyses either for K^{39} (chemical) or K^{42} (physical) do not reveal the nature of the events; only by simultaneous analyses for both may the situation be depicted.

system is, of course, not really motionless except at absolute zero, as Brownian movement and infra-red emission dissipate the thermal energy of the solution at room temperature. If it were possible to introduce into this apparently motionless system, without disturbing it, a droplet of $K^{42}Cl$, the K^{42}:K^{39} ratios in any area of the solution rapidly would become constant, as an expression of the attainment of physical equilibrium.

Early physicists who studied the difficulties of attaining and maintaining a vacuum, stated that, "Nature abhors a vacuum." This might be paraphrased to state that, "Nature abhors the separation of isotopes." Energy must be expended to separate isotopes of the same element; and, given an opportunity to do so, the separation will yield again to proportional distribution.

If the droplet of $K^{42}Cl$ introduced were in the form of a globule surrounded by a permeable membrane, and containing within it a KCl solution of exactly the same concentration as that in the beaker, the same equilibrium would occur. But the amount of KCl in the globule would not be altered. Physical equilibrium has taken place without chemical transport; by way of analogy, the radiosodium has disappeared from the gastric pouch without necessarily indicating any net absorption of sodium. Atoms have moved, not milliequivalents. Actually the disappearance of K^{42} from the globule of KCl in the beaker is a measure of *permeability to*, not *transport of*, the ion, using the term "transport" to mean the movement of enough atoms to alter the chemical concentration of the total isotopic mixture on one side or the other of the membrane in question.

This confusion of physical equilibrium with chemical transport may be a source of error in the interpretation of results; only by concomitant measures of radioactive and stable isotopes (i.e. physical and chemical analyses) and the calculation of specific activity may such confusion be avoided (Figures 1, 2, 3 and 4).

3. Phase measurements. The use of isotopes to measure areas of body water or the total

[1]This and the subsequent chart are based on work now in progress under contract with the Office of Naval Research and Harvard University.

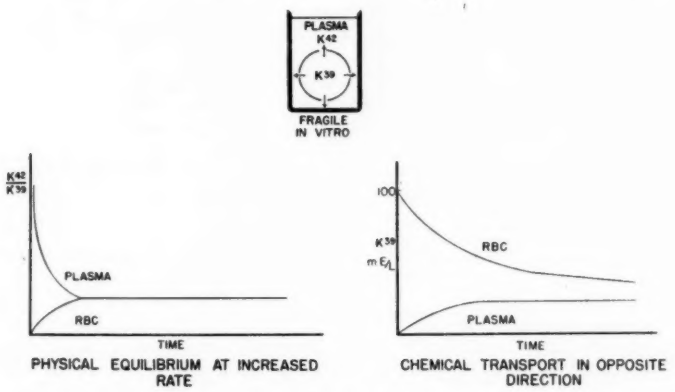

Fig. 4. Diagrammatic representation of a biological situation analogous to that shown in Figure 2, and in contrast to that shown in Figure 3. The poorly preserved erythrocyte, *in vitro*, is releasing its potassium as a preliminary (or accompaniment) of hemolysis. The K^{42} added to the system still enters the red cell, and with an increased rate, as normal permeability relationships are upset by the "death" of the cell. As in Figure 2, net chemical transport (concentration or distribution alteration) is taking place in a direction opposite to that taken by the "tracer." Only by concomitant physical and chemical determinations may such a situation be revealed. It is of interest that the nonviable erythrocyte appears to have lost its non-exchangeable moiety of intracellular potassium.

amount of solid bodily constituents involves a simple concept, the formula for which is illustrated by analogy in Figure 6. The accuracy of this determination will depend upon the statistical accuracy of the "specific activity" figure employed in the final ratio; in terms of Figure 6, the ratio of black to white apples in the "fair sample" taken after mixing.

This method may be used to serve three types of application in biological research. The first involves the use of nonisotopic materials for the measurement of fluid volumes; the second involves the use of isotopes for the measurement of fluid volumes; and the third embodies the use of isotopes to measure the total quantity of certain solid (ionic or elementary) constituents of the body.

In the *measurement of areas of body fluid*, calculation depends upon the familiar formula for dilution:

$$C_1V_1 = C_2V_2$$

where C_1 and V_1 represent the concentration and volume of solute in solvent before dilution, and C_2 and V_2 after dilution. C_1 and V_1 are known to begin with, C_2 is measured after mixing, and V_2 may be calculated:

$$V_2 = \frac{C_1V_1}{C_2}$$

The use of dyes to measure plasma volume is the earliest and most widely used application of this principle to biological work; it dates back to the work of Keith, Rowntree and Geraghty (41). When this method is used the "tracer" is detected by color instead of by radiation or weight and constitutes a tracer not because it resembles any of the normal constituents of the plasma (though Evans blue has colloidal properties not unlike albumin in aqueous solution) but because it is a dye which forms a nonpolar bond with plasma protein (largely albumin) at low temperatures (5, 57). It, therefore, in actuality measures the "albumin space," and its complex disappearance curve is partly the result of the fact that a significant moiety of plasma albumin circulates outside the plasma.

Ideally, the perfect tracer to use in measuring a body fluid space is an isotope of a normal constituent of that space, which rapid-

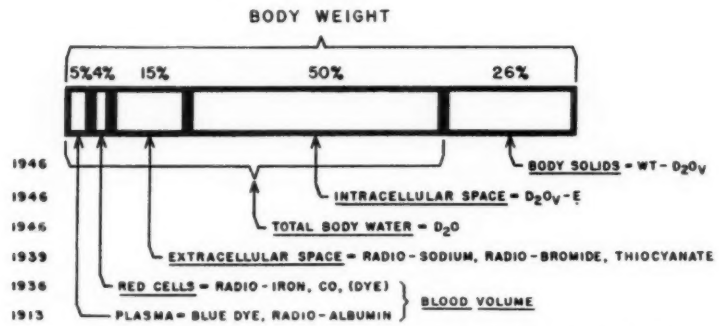

Fig. 5. Diagram illustrating some of the methods now available for the measurement of "phases" of the body fluids. References to the technical procedures involved are to be found in the text.

ly equilibrates in the total isotopic mixture and, after an initial mixing phase, presents a "flat" disappearance curve at any point in which a fair sample may be removed to determine C_2 and solve the equation for V_2. Though the dye departs widely from this theoretical ideal, its extensive use and study by Gibson, Gregersen and others has rendered it a highly useful device (2, 24, 27, 28, 37, 38).

The employment of thiocyanate ion is another nonisotopic application of this principle used to measure the volume of extracellular fluid available for thiocyanate solution (14, 20, 29). Thiocyanate is an anion similar in many respects to chloride and used, in essence, as a tracer for chloride. It is determined chemically by colorimetry. Like the dye, it is foreign to the body (though some individuals may carry basal concentration of 0.2-1.0 mgm. per cent, a fact which must be determined in all SCN space measurements) and in addition it is slowly removed and may be toxic in high concentration. Repeated determinations leave residual quantities in the serum, which render each successive determination less accurate as the injected quantity constitutes a progressively lesser increment over the basal concentration.

The use of radioactive isotopes of iron (as hemoglobin synthesized in a donor who has been given the radio-iron) to measure the red cell mass, is a theoretically perfect application of the tracer principle to a space measurement (25, 26, 51, 55). The radioactive iron-containing red cells from the donor mix with the recipient's cells like the apples in the barrel; they do not escape into other compartments, and the disappearance curve is essentially flat for long periods, being affected only by cell destruction or the slow formation of new cells from dietary iron. From a practical standpoint, the chemical processing to which the cells must be subjected prior to electroplating, and the weak x-ray emitted by Fe^{55} which makes detection difficult, contrive to render this method cumbersome although widespread investigative application is feasible.

The use of Na^{24} to measure the extracellular fluid—the sodium space—is practical and readily available (39, 69). From a theoretical point of view, it is not perfect since after initial mixing the disappearance curve is not flat but drops slightly as sodium penetrates cells and is incorporated into bone. Just as with the dye-plasma method, this "leakage" of the tracer into another area may be compensated by adopting a standard sampling time early in the curve.

The use of deuterium for measurement of total body water is another "ideal" application of the tracer principle to body fluid space measurements (34, 35, 42, 49, 50, 54). Although deuterium has twice the mass of H, this weight difference does not appear to interfere with applicability; the use of H^3 might be seriously hampered by this mass

change.[1] Deuterium exchanges with the exchangeable hydrogen in organic compounds as well as with H_2O; but this amount is quantitatively so small as compared with the great volume of body water that it escapes measurement unless one isolates the end-products of that exchange or the compounds synthesized by the body in the presence of deuterium-rich H_2O. The physical apparatus necessary to measure plasma-deuterium by gravimetric means is not complicated, and the measurement of total body water by this technique is available now that D_2O has been released for general use by the Atomic Energy Commission.

The measurement of *total solid constituents* by the use of isotopes involves the same fundamental considerations; the "concentration," however, is not the radioactivity per unit volume of solvent but is instead the actual isotopic concentration—the radioactivity per unit weight of isotopic mixture—in short, the "specific activity," (50). Thus C_1V_1 becomes the total radioactivity injected, C_2 the specific activity after equilibrium has occurred, and V_2 the total amount (in terms of weight) of isotopic mixture in which the isotope has become mixed.

The measurement of total body sodium by this method consists in measuring the specific activity of the plasma sodium after equilibrium has been attained (24 to 36 hours) and dividing this ratio into the total activity injected at the outset. The urinary excretion should be subtracted from the injected activity; the quantity excreted in the case of radiosodium is small.

Total body potassium may be measured by the same technique, though urine excretion is significant and must be measured. The selection of what constitutes a "fair sample" of exchanged potassium is more complex. Studies now under way in this laboratory on K^{42} at equilibrium with K^{39} in the human body indicate that the urine specific activity after 30 hours represents exchange conditions throughout the body, providing that dietary

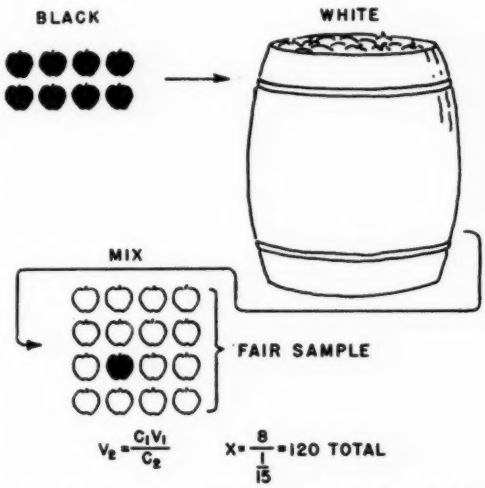

Fig. 6. An analogy devised to illustrate the principle involved in the determination of total exchangeable constituents by the tracer method.

The number of white apples in the barrel is unknown. A known number of black apples similar in size and shape, the "tracers," are added to the system. Mixing is produced, and a "fair sample" is then removed for examination. The ratio of black to white apples is determined, and from this ratio the total number of apples in the barrel is calculated as shown.

In the biologic experiment, the unknown number of apples finds its analogy in the total quantity of ions to be measured; the "tracer" is the isotopic material to be mixed in the body; the "fair sample" is the tissue or fluid measurement made at equilibrium; and the ratio of black to white apples is the "specific activity" under equilibrium conditions. The final calculation consists in dividing the specific activity into the total activity present in the organism, to determine the total quantity of ion with which the isotope has exchanged.

K is limited prior to measurement of the urinary specific activity. The red cell, originally conceived as a satisfactory "barometer" of the K^{42}:K^{39} ratio at equilibrium, has been found to be unsatisfactory because of the apparent presence therein of nonexchangeable or slowly exchangeable potassium. Muscle, liver, plasma and urine are in equilibrium after 24 hours (16, 18, 22, 53, 70). Muscle and liver are, of course, not readily obtainable for sampling. Plasma, because of its low K^{39} content, has low K^{42} values under conditions of physical equilibrium. The urine, therefore, constitutes the most readily available source of K for study of K^{42}:K^{39} ratios and calculation of total exchangeable K.

[1]The work of Pace, et al. (J. Biol. Chem., 1947, 168:459) employing "tritiated water" (HTO) to measure the total body water suggests that hydrogen of mass 3 is satisfactory from a practical viewpoint despite the theoretical objection raised by the mass increment.

Dietary K finds a high representation in urinary K because the excretion rate of K is directly proportional to the plasma concentration over about 5 mE/L (71). For this reason the total body (exchangeable) K measurements must be made after a 12 hour K-free fast—an overnight fast being sufficient for this purpose.

Methods for the measurement of total exchangeable nitrogen, carbon, sulfur, and phosphorus could similarly be worked out; in each case special problems of determining C_2 and the exact anatomicochemical extent of V_2 will arise and must be settled to establish the validity of the result.[1]

The application of these measurements of "total body constituents" to the pressing problems of surgical nutrition and preoperative and postoperative care may lead us to a more quantitative concept of the needs of the surgical patient.

SUMMARY

1. Some practical problems relative to the biological use of isotopes are briefly discussed.

2. An increasing application of these methods to the problems of surgery may be expected in the future.

3. Such application will be most fruitful if adequate attention is paid to the fundamental biology of the problem at hand and to the basic considerations relative to all isotope research.

[1]The work of Wintrobe and his group (*J. Biol. Chem.*, 1946. 165: 397) on the "labile iron pool," measured by the dilution of radioactive iron, represents an extension of this principle into the complex problems of iron distribution and metabolism; the measurement is essentially that of the "total exchangeable iron."

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THE RECTOGENITAL SEPTUM

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CAUDAL to the peritoneum of the rectovesical pouch in the male, the rectum and the bladder (together with seminal vesicles and prostate gland) are separated from one another by a relatively thin layer of tissue. In this tissue is found a membranous septum, which is closely attached, by its cranial margin, to the peritoneum at the bottom of the rectovesical pouch, and adheres, by its caudal end, to the dorsal surface of the prostate gland. For this membrane, the term of "rectovesical septum" has been in use for some time in conventional anatomy.

A similar septum is found almost without exception in the female between the rectum and the vagina; in conformity with the nomenclature employed in the case of the male, it should be called the "rectovaginal septum." To denote the male and female septa collectively, we will use in this article the term of "rectogenital septum."

For several reasons this septum is of considerable importance. In the first place it separates the rectum from the bladder, seminal vesicles, and prostate gland in the male, and from the vagina in the female. And furthermore it is to be counted among the structures which constitute the supporting mechanism of the genitourinary organs. Finally, as will be discussed in another article, this septum, in combination with certain fascial sheets, effects a complete division of the subperitoneal space of the pelvic cavity into a dorsal or rectal compartment and into a ventral or urogenital compartment.

Concerning the nature of the rectogenital septum two opinions are in existence; according to one of them it is of peritoneal origin, while according to the other one it would be a purely fascial structure.

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Briefly the history of our knowledge of the rectogenital septum is as follows. The tissue between the rectum and bladder in the male was investigated first by Denonvilliers in 1836; hence urologists are still using the term "Denonvilliers' fascia" for this tissue in the male. Later on, in 1899, two other Frenchmen, Cuneo and Veau studied the "fascia prostatoperitonealis" from an embryological point of view and arrived at conclusions which, in the opinion of the authors of the present article, are valid up to the present day. According to Cuneo and Veau the prostatoperitoneal fascia (our rectovesical septum) is a peritoneal derivative and results from the fusion, during embryological development, of the ventral with the dorsal wall of the rectovesical pouch which in early embryological stages extends all the way down to the pelvic floor. In 1922, Miley B. Wesson reinvestigated the rectovesical septum and refuted the views advanced by Cuneo and Veau. On the basis of embryological studies this author claimed that the rectovesical septum is of fascial nature. The most recent publication on this subject is an article by Tobin and Benjamin and represents again an embryological investigation the results of which, however, were confirmative of the interpretation which Cuneo and Veau gave to the rectovesical septum.

Another quite recent article (1940) must be mentioned here. As we will see later on, we have never had any difficulty, either in the student dissecting room or in special dissections, to display the rectovaginal septum in the female cadaver. Curtis, Anson, and Beaton, however, were evidently not able to find a rectovaginal septum. On p. 649 (2) they describe the tissue located between the rectum and the vagina as being composed of the fascial envelopes of rectum and vagina, with some "cellular tissue" intervening between them.

Since certain observations in adult cadavers seemed corroborative of the views of Cuneo and Veau, the senior author of this article has long been accustomed to teach the subject of the rectogenital septum to his students in the light of the studies made by these two French anatomists. Later on, however, when we became familiar with Wesson's article refuting the peritoneal theory of the rectovesical septum, we found it necessary to reinvestigate this problem and, more especially, to record our observations by suitable illustrations. Since 1939 we have collected a large number of observations, some of which will be reported in the present article.

It is our object to report, in the first place, certain details which can easily be observed in adult cadavers and which can best be explained in the light of the peritoneal origin of the rectogenital septum. In the second place, some observations in infants will be discussed, which show that even during late intrauterine life the rectogenital pouch continues to recede from the rectogenital space.

OBSERVATIONS IN THE ADULT

Our attention was devoted mainly to the relation between the rectogenital septum and the peritoneum of the rectogenital pouch and further to the configuration of the peritoneum along a line corresponding to the attachment of the septum. But incidentally we also have made measurements to determine how far caudally the rectogenital pouch extends.

1. *Caudal extent of rectogenital pouch.* It is generally assumed that in the female the rectovaginal pouch reaches down further caudally than the rectovesical pouch does in the male. On the average the bottom of the rectovesical pouch is said to lie 3 inches above the anus, the bottom of the rectovaginal pouch only 2 inches. Because of the scarcity of female cadavers we had no opportunity to study the variations in the level of the rectovaginal pouch. In one female, illustrated in Figure 5, a colored woman, 29 years old (479$_{42}$, 1946), the bottom of the rectovaginal pouch was located 35 millimeters cranial to the ventral commissure of the anus. In another female cadaver (479$_{38}$, 1944), of a colored woman aged 35 years (see Fig. 6), only the distance between the bottom of the pouch and the pelvic floor was measured; it was 58 millimeters, i.e. over 2 inches; to conclude from this value, the bottom of the rectovaginal pouch in this female must have been located nearly 3 inches cranial to the anus, i.e. nearly twice the distance which it had in female 479$_{42}$, 1946.

TABLE I.—VARIATION IN DEPTH OF RECTOVESICAL POUCH IN THE ADULT MALE[1]

No. of specimen	Distance from bottom of rectovesical pouch to anterior anal commissure—mm.
1	58
2	70
3	
4	76
5	78
6	62
7	
8	75
9	74
10	78
11	58
12	58
13	
14	68
15	50
16	64
17	57
18	68
19	62
20	34
21	48
22	48
23	68
24	75
25	54
26	65
Greatest length	78.
Shortest length	34.
Mean length	63.1
Median length	56.

[1]The measurements were made by Mr. Allen Benson Spanier January, 1947, in cadavers of the student laboratory.

In males we have made a larger number of measurements. In Table I the cranial distances of the bottom of the rectovesical pouch from the ventral commissure of the anus, as measured in midsagittal section through the pelvis, are listed for 23 male pelves. One glance suffices to make one realize that the variability of this value is very considerable (from 34 to 78 mm.). Only in 6 among the 23 cases, the bottom of the rectovesical pouch was found 3 inches or slightly more (74 to 78 mm.) cranial to the anus. In 8 cases the pouch was located only about 2 inches (from 48 to 58 mm.) above the anus, and in 1 case this distance was only 34 millimeters (1½ inches) i.e. less than the assumed average in the female.

TABLE II.—LEVELS OF BOTTOM OF RECTOVESICAL POUCH (in mm.) IN THREE MALE CADAVERS OF

Series 47941, 1945*

	Cranial distance from ventral commissure of anus	Cranial distance from tip of coccyx†	Caudal distance from tip of coccyx‡	Cranial distance from pelvic floor	Cranial distance from cranial end of prostate	Caudal distance from cranial end of prostate
47941 d	95					
47941 f	110	23		57	25	
47941 j	61		22	21		35‡

*47941 d is illustrated in Figure 4; 47941 f in Figure 3; and 47941 j in Figure 1.
†Tip of coccyx, i.e. a line connecting the tip of coccyx with the ventrocranial end of the symphysis pubis.
‡No rectovesical septum was present in this subject.

In 3 other males (Series 47941, 1945), listed in Table II, 2 had values (95 and 110) much above those recorded in Table I. In one of them (47941 f) the distance between the bottom of the pouch and the anus was nearly 4½ inches.

On the whole these measurements show that in operations necessitating perineal access to the pelvic viscera, no reliance can be placed upon average figures which express the distance from the anus at which the operator may encounter the bottom of the peritoneal cavity. A more reliable information may be obtained from the relation between the skeleton and the bottom of the rectogenital pouch. In observations made in the student laboratory, extending over many years, we found that the bottom of the rectovaginal pouch of the female lies almost invariably caudal to the tip of coccyx. This relation existed in both females to be described in this article; in 1 of them (47942, 1946), illustrated in Figure 5, the distance between coccyx and rectovaginal pouch was measured, and it was found that the bottom of the pouch was located 15 millimeters (i.e. slightly more than half an inch) caudal to the tip of the coccyx.

In the male the bottom of the rectovesical pouch, on the contrary, lies almost invariably above the tip of the coccyx, opposite the fourth or fifth piece of the sacrum. We found, however, one male subject (47941 j, 1945), illustrated in Figure 1, and listed in Table II, in which the bottom of the pouch was located 22 millimeters (i.e. nearly 1 inch) below the tip of the coccyx.

Another relationship, more reliable than the distance of the pouch above the anus, is the relation of the pouch to vagina and prostate gland. In most adult females the bottom of the rectovaginal pouch lies just opposite the dorsal fornix of the vagina, only a narrow strip of the most cranial end of the dorsal vaginal wall being covered by peritoneum. Even in the female 47942 (illustrated in Fig. 5) in which the bottom of the pouch extended exceptionally close to the anus, only the most cranial 8 millimeters of the dorsal wall of the vagina were covered with peritoneum. Similarly in the male the bottom of the rectovesical pouch lies in the great majority of the cases well above the cranial end of the prostate gland. An exception of this rule was the male 47941 j (illustrated in Fig. 1); in this subject the rectovesical pouch extended to nearly the middle of the total length of the dorsal surface of the prostate gland; 35 millimeters of the gland were covered with peritoneum.

2. *Configuration of peritoneum at bottom of rectogenital pouch.* An examination of the peritoneum of the bottom of the rectogenital pouch reveals certain features which are the direct result of the fusion of the dorsal and ventral walls of the pouch with one another.

In Figure 1 the right half of the male pelvis (47941 j), repeatedly referred to above and recorded in Table II, is illustrated. It represents a case in which the bottom of the pouch was situated exceptionally far caudal in relation to the prostate gland. If it is true that the rectovesical septum is the result of the fusion of the peritoneal walls of the rectovesical pouch, one might expect that in cases of an exceptionally far caudal situs of the pouch the rectovesical septum might be completely missing. This condition existed actually in this male subject. The pouch was fixed to the pelvic floor merely by a mass of unorganized

connective tissue. Moreover, careful examination of the inner surface of the peritoneum at the bottom of the pouch failed to reveal any special features of this peritoneum, such as are found when a septum is present, and will be discussed in the following paragraphs.

In Figure 2, the right half of the pelvis of a white male, aged 69 years (479II a, 1945) is illustrated. In this subject the bottom of the pouch was located well above the prostate gland. Attached to its outer surface is seen the rectovesical septum which could be displayed with great ease and perfectly clearly. As is always the case in the male it was separated from the rectum by a quantity of loose connective tissue which could be easily broken down with the finger. Ventrally it was more closely adherent to bladder and seminal vesicles; from these structures it was raised with the aid of a blunt instrument as far caudal as the prostate gland. On the dorsum of the gland it faded away into the fascial capsule of this organ. Inspecting the peritoneum of the pouch on its inner (cranial) surface, we observed, running transversely and corresponding to the line of attachment of the rectovesical septum on the outside, a slightly grooved line of whitish color, which resembled a scar such as remains after a surgical suture. Along this line and on either side of it, the peritoneum was slightly wrinkled perpendicularly to the line. This configuration of the peritoneum is particularly conspicuous, as everywhere else in the pouch the peritoneum is perfectly smooth and devoid of irregularities. As is usually the case, the scar-like line extended laterally on either side where the walls of the pouch rise along the lateral walls of the pelvis, corresponding to a cranial continuation of the rectovesical septum into "lateral peritoneal wings" of the pouch. As has been described in another article (6), these lateral wings serve for the attachment of the peritoneal pouch to the visceral endopelvic fascia. The location and direction of the line, both corresponding to the line of attachment of the rectovesical septum, as well as the appearance of the peritoneum along this line, leave no doubt that it represents the line along which the dorsal and ventral walls of the pouch fused with one another.

Another similar case, but with the line of fusion even more conspicuous, is illustrated in Figure 3; it pictures the right half of the pelvis of a male negro (479II f, 1945) aged 51 years (measurements recorded in Table II). The rectovesical pouch was located well above the prostate gland (25 mm.) and a well developed rectovesical septum was present. Again a whitish scar-like line was present on the inner surface of the pouch, which corresponded in location exactly to the line of attachment of the rectovesical septum on the outside. In this case the whitish line was even more conspicuous than it was in the previous case, as it was more irregular and crossed in several places by cord-like thickenings of the peritoneum. From its midpoint in the median sagittal plane it extended laterally on either side for a distance of 41 millimeters, having thus a total length of about $3\frac{1}{5}$ inches.

There is another feature which is shown in this illustration. We made a special attempt in the dissection of this pelvis to ascertain the relation between the rectovesical septum and the fascial capsules of rectum and bladder. As is shown in the illustration, each of the three membranous structures was dissected and displayed individually. As in the previous case the rectovesical septum was closely adherent to the bladder and prostate gland, but was separated from the rectum by loose connective tissue. It could be followed, as an individual sheet of tissue all the way down to the pelvic floor; cranially it was continued without any discernible boundary or change in texture, into the peritoneum of the rectovesical pouch. With similar distinctness we were able to display the fascial capsules of the rectum dorsally and of the bladder and prostate gland ventrally. Contrary to the description given by Curtis, Anson, and Beaton for the female pelvis, the rectovesical septum is a structure additional to, and independent of, the fascial capsules of the adjacent viscera. Attention should be called also to a condition of the capsule on the ventral surface of the rectum, which we have encountered in many other cases. The ventral capsule of the rectum as shown in Figure 3 was attached cranially to the peritoneum of the rectovesical pouch, slightly above the line of attachment of the

septum. From this level on, cranially, the ventral capsule of the rectum, if there was one, could not be displayed, gross-anatomically, as a layer independent of the peritoneal covering of the rectum. In connection with this condition it should be pointed out that the rectovesical septum could be distinguished clearly from the fascial capsules; as will be referred to again, its texture and color were different from those of the fascial sheets.

In Figure 4 (47941 d, 1945) an extreme case of the "scar" at the bottom of the rectovesical pouch is illustrated (for measurements see Table II). In this subject, a colored male aged 47 years, this line extended far laterally rising up cranially along the lateral wall of the pouch, where on the outside a well developed lateral peritoneal wing was attached to the pouch, its line of attachment corresponding exactly to the location of the linear "scar." While elsewhere in the pouch the peritoneum showed a perfectly smooth surface, it was thrown, along the whitish line, into many wrinkles and coarse folds running perpendicular to the line and creating the impression that some secondary processes of reorganization had taken place in this region during development. In addition a series of strong peritoneal cords had developed which were running in dorsoventral direction, bridging over the line of fusion. Obviously these cords must have had the effect of re-enforcing the line of fusion, preventing a secondary splitting of the septum into its two original layers. Seeing this line and its accessory formations in a specimen as the one described above, one could not be in doubt that the rectovesical septum is the result of fusion of the dorsal and ventral walls of the rectovesical pouch with one another. This line corresponds exactly to the line of attachment of the septum, it is the only place in the pouch where the peritoneum is not smooth, and the peritoneal structures developed along this line have the effect of preventing a reopening of the fused portion of the pouch.

The rectovaginal septum of the female pelvis is illustrated in Figure 5, picturing the left half of the pelvis of a colored female (47942 a, 1946) aged 29 years. In this subject, however, the mode of attachment of the septum to the peritoneum differed from the specimens described previously. The peritoneum at the bottom of the pouch was carefully examined, but neither the whitish "scar" nor any other signs of processes of reorganization could be detected. The cranial end of the septum was split into two leaves, a ventral and a dorsal leaf; each of these was attached separately and was continued, without discernible boundary, into the ventral and dorsal wall, respectively, of the rectovaginal pouch. Across the gap between the two limbs, the peritoneum of the pouch had grown as a continuous peritoneal partition, separating the space of the gap from the peritoneal cavity and, at the same time, re-enforcing the line of fusion in the manner of a binder. Obviously this is only a special case of the peritoneal cords. Instead of cords isolated from one another by varying intervals, the peritoneum had grown over the gap between the two leaves of the septum as one single continuous sheet.

As in the male, the fascial capsules of the viscera adjacent to the septum could be displayed as structures entirely separate from the septum (Fig. 5). Moreover, as in many males, the ventral capsule of the rectum was attached cranially to the peritoneum of the pouch and could not be demonstrated, cranial to this level, as an individual layer. As the illustration shows, the same condition existed with respect to the capsule of the vagina; beyond the level of its attachment to the peritoneum of the pouch, over the body and fundus of the uterus, no individual capsule could be demonstrated, a condition which, however, is well known.

We observed in this specimen, before any dissection was made, that the rectovaginal septum passed from its cranial attachment forward to the dorsal wall of the vagina to which it was closely adherent, while dorsally it was separated from the rectum by a considerable space filled in with loose connective tissue. When the uterus and with it the vagina were pulled forward, the septum followed the vagina; it was not held to the rectum. This close relationship of the septum to the genitourinary viscera in both sexes is of considerable importance. If a finger is introduced through a transverse perineal incision, preparatory to creating access to the pelvic viscera, the oper-

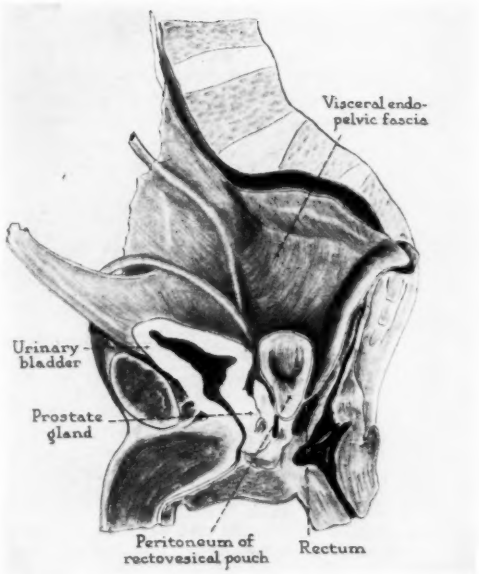

Fig. 1. Right half of pelvis of a male negro (479$_{41j}$, 1945), 60 years of age, seen in medial view. A case in which the rectovesical pouch descended as far caudal as the middle of total length of dorsal surface of prostate gland and in which the rectovesical septum was missing.

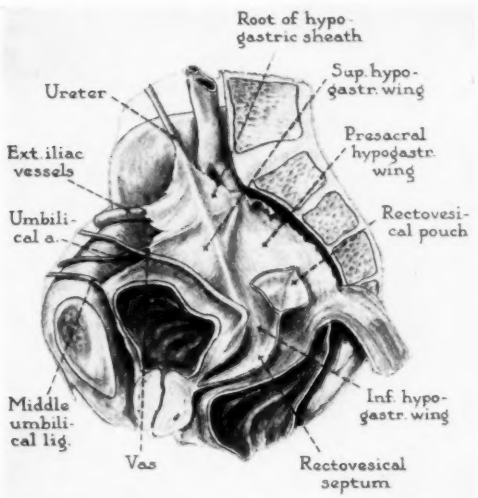

Fig. 2. Right half of pelvis of a white male (479$_{41a}$, 1945), aged 69 years. Peritoneum has been removed everywhere except for the rectovesical pouch and septum. The hypogastric sheath is seen in its entire extent. The vas deferens passes across the superomedial surface of the superior hypogastric wing and is thus excluded from the space of Retzius. (This figure is same as Figure 6a in article entitled "Visceral Endopelvic Fascia," *Surg. Gyn. Obst.*, 1948, 86: 9–28.)

ator may feel reasonably certain that his finger will be separated from the genitourinary organs by the rectogenital septum, but will be in immediate contact with the ventral capsule of the rectum.

In Figure 6, a dorsal dissection of the pelvis of a colored female (479$_{38}$, 1944), aged 35 years, is illustrated. The coccyx and levator ani as well as the rectum had been removed. Both the ventral and dorsal fascial capsules of the rectum and their lateral expansions are still visible. The dorsal wall of the rectovaginal pouch and the rectovaginal septum are exposed to view. The rectovaginal septum was incised longitudinally and reflected to either side; this manipulation exposed the dorsal capsule of the vagina; upon incision and retraction of it the musculature of the vagina came into view.

By undermining the space between the septum and the vaginal capsule and the space between the rectal capsule and the septum, the latter could be followed all the way down to the pelvic floor; its length from the line of attachment to the pouch down to the pelvic floor was 58 millimeters (as compared to 30 millimeters in the female discussed previously).

At first we were unable to see a boundary line between the septum and the dorsal peritoneum of the pouch. From outside the two looked alike, but could be distinguished from the fascial sheets. Gradually as the specimen was worked on and the peritoneum and septum were pulled and stretched in different directions, a faint line which gradually became more pronounced, was discovered; it was crossed by a number of what appeared to be fascial strands. Even then complete certainty could not be obtained, until we introduced the handle of a scalpel through an incision in the dorsal wall of the pouch; this procedure permitted exploration of the pouch and exact determination of the line along which the septum was attached to the pouch.

Exactly as inspection of midsagittal sections, complete dissection from the dorsal side

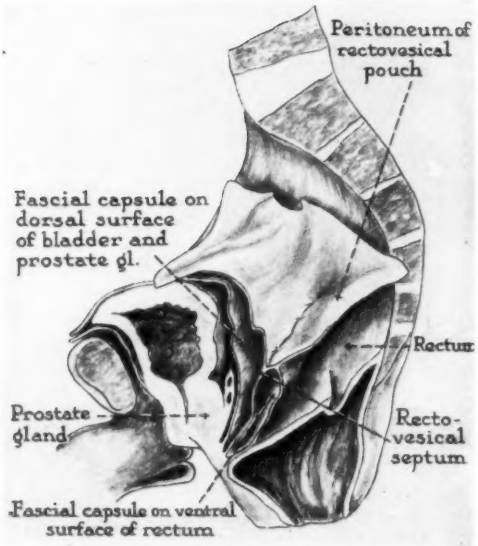
Peritoneum of rectovesical pouch
Fascial capsule on dorsal surface of bladder and prostate gl.
Rectum
Prostate gland
Recto-vesical septum
Fascial capsule on ventral surface of rectum

Fig. 3. Right half of the pelvis of a male negro (479III, 1945), aged 51 years, seen in medial view. Note the line running transversely across the bottom of the rectovesical pouch, and several wrinkles in the peritoneum, running perpendicular to the line. Observe that the fascial capsule of the rectum and that of the bladder and prostate are structures independent of the rectovesical septum. (Illustrated by John L. Moyer.)

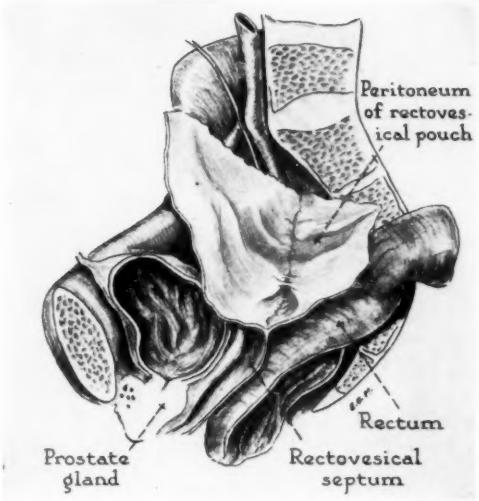

Fig. 4. Right half of pelvis of male negro (479IId, 1945), aged 47 years, seen in medial view. Note the linear scar running transversely across the bottom of the rectovesical pouch; observe the folds and wrinkles of the peritoneum along the scar and peritoneal cords bridging over scar.

leads to the conclusion that the rectovaginal septum is a structure of real existence, that it is continuous with the peritoneum of the rectogenital pouch but is entirely independent and different from the fascial capsules of the adjacent pelvic viscera.

3. *Peculiarities of the rectogenital septum.* The cases of rectogenital septum discussed in the preceding paragraphs were especially selected because they are among those which have a bearing on the developmental origin of the septum; many similar examples have been found over a period of many years in the student dissecting room and in special dissections. These cases, however, do not convey an idea of the great variability of the septum with respect of its completeness. It has already been mentioned that in rare cases the septum may be entirely missing. But there are instances in which the septum is perforated by holes in a varying degree, and other instances in which it no longer impresses as a sheet but consists of a number of separate narrow strips which become very thin caudally and fade away on the bladder, prostate gland, or vagina. This variability in completeness explains some of the differences of description found in the literature as well as the failure of some authors to find such a septum.

Nevertheless if a well developed septum is present, it can be easily distinguished by gross examination from the surrounding fascial tissues. The fascial sheets of the visceral capsules, while they represent definite membranous envelops, nevertheless, evoke upon touch the feeling of a more loosely woven material, of felt-like nature; the surfaces of these capsules are rough, of whitish color and of dull appearance. The septum, on the contrary, does not feel fibrous; it feels to the fingers like a smooth and firm, densely woven material. Moreover, in many cadavers, the surface of the septum has a distinct luster of slightly bluish tint. In several instances the septum stood out prominently by a faint, but distinct greenish color, similar to that of bile; so far, however, we are uncertain concerning the source of this pigment.

In the male cadaver 479II a, 1945 (illustrated in Fig. 2), the pouch, together with the cranial half of the septum, was removed, placed in alcohol and examined later under a binocular dissecting scope. The outer surface of the septum and of the peritoneum of the pouch was covered by a thin layer of brownish colored areolar tissue of loose texture through which the peritoneum and septum could be seen in many places. After this outer layer had been removed, the surface of the remaining parts appeared slightly bluish to the naked eye. The septum consisted of coarse, flat, ribbon-like fibers of considerable width and of a bluish and glistening surface; they were wrinkled cross-wise as if they had shrunk by retraction of some elastic material within them. All of these fibers were running in craniocaudal direction (from the pouch toward the pelvic floor) and were arranged in two layers easily separable from one another. The fibers of each layer were continued upon the outer surface of the corresponding wall of the pouch, where they gradually faded away in the peritoneum. Close to the bottom of the pouch these fibers were more densely placed than farther caudally; many of them, however, extended through the whole length of the septum, as far caudal as the cut edge of the septum where they were cut off. The spaces between the fibers were filled in by a delicate and transparent loose connective tissue.

In many instances the rectogenital septum may be easily and neatly split into a dorsal and a ventral leaf. This we have demonstrated to our students for many years and we advise them routinely to attempt a separation of the septum into its two original layers. Pelves that have been halved by a midsagittal section are especially suitable for this purpose. Running the handle of a scalpel repeatedly along the white line on the inner surface of the pouch and exerting at the same time cautious pressure will frequently accomplish the desired result. In cases of the presence of peritoneal cords bridging over the scar, these cords must be carefully cut through. In the dorsal dissection illustrated in Figure 6, an attempt to split the septum was made and succeeded very easily.

Fig. 5. Part of left half of pelvis of colored female, picturing rectovaginal septum and its relationship to capsules of rectum and vagina. Peritoneum left intact. (This is same as Figure 2 in article entitled "Visceral Endopelvic Fascia," *Surg. Gyn. Obst.*, 1948, 86: 9–28.)

It seems that under certain conditions splitting of the septum and reopening of the pouch can occur in life. In this connection a report published by J. M. H. Rowland in 1926 on a case of extrauterine pregnancy is of interest. The embryo developed entirely in the peritoneal cavity, dorsal to the uterus. At term the head of the child which was delivered by cesarean section, was found in the pouch of Douglas where it had moved all the way down to the floor of the pelvis. No break in the peritoneal lining of the pouch was found. The weight of the fetus evidently had split and separated the two layers of the septum, thus reopening the pouch to its original caudal extent.

OBSERVATIONS IN INFANTS

Of the infants which we examined, 37 will form the subject of this article.

Only in a single one (dissection 48, 1946, colored female infant, full term, dissected by Dr. R. M. Cunningham) of these 37 infants did the rectogenital pouch extend all the way down to the pelvic floor. It was dissected from the dorsal side; after removal of the sacrum, coccyx, and rectum, together with the dorsal

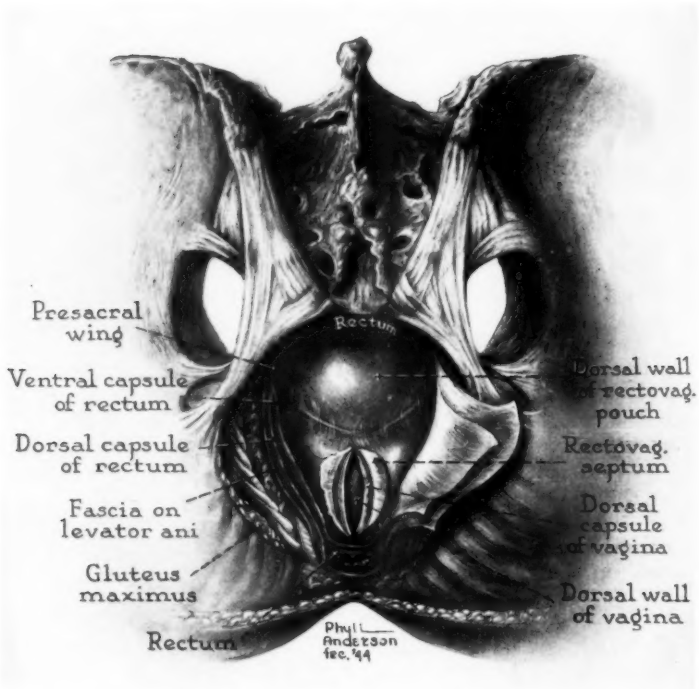

Fig. 6. Dorsal dissection of pelvis of a colored female (479$_{38}$, 1945), aged 35 years. Coccyx, levator ani, and rectum have been removed. Dorsal and ventral leaves of fascial capsule of rectum were incised longitudinally; on the left side they are shown cut away, on the right side they are reflected to the right. The rectovaginal septum is seen from its dorsal aspect; through a longitudinal slit in it the capsule and muscular wall of the vagina are visible.

wall of the rectovaginal pouch, the ventral wall of the pouch was exposed in a dorsal view (Fig. 7). The peritoneum is seen to cover the entire dorsal wall of the vagina from which it is reflected at the level of the pelvic floor. While this infant does not represent an early fetal stage (it is a full term baby), it is noteworthy that we have never encountered this condition in adult cadavers.

Of the remaining 36 infants which are recorded in Tables III and IV, we made measurements to ascertain the level of the bottom of the pouch in relation to certain landmarks. In both sexes—there were 20 males and 16 females—four measurements were taken from each specimen. The landmarks which were used as measuring points, are shown diagrammatically in Figures 8 and 9.

In not one of the 36 recorded infants did the peritoneal pouch extend to the floor of the pelvis, although the youngest among them were only 6 month intrauterine age and, with few exceptions, a rectogenital septum was already present, resembling the rectogenital septum of the adult. In Figure 10 (479$_{4}$, 1943) a sagittal section through the pelvis of a representative case is illustrated. The rectovaginal pouch is seen, as well as the rectovaginal septum which was continued uninterruptedly into the peritoneum at the bottom of the pouch. In Figure 11 (479$_{26}$, 1943) a sagittal section through the pelvis of a male infant is illustrated, in which no septum was present. From the ventral wall of the rectovesical pouch a hollow spur was projecting in caudal direction; it is possible that this was the beginning of the proc-

esses leading ultimately to the formation of the septum. This infant, however, did not represent a particularly early stage; its intrauterine age was 7.8 months and its crown-rump length 26.5 centimeters. The bottom of the pouch extended unusually far caudally; it was situated below the level of the caudal end of the prostate gland. As has been mentioned, there are few adults in which the septum is missing (Fig. 1).

In Figure 12 a midsagittal section through the pelvis of a male infant (479_{30}, 1943) is diagrammatically illustrated; among the 20 male infants recorded in Table III, it was one of the two in which the rectovesical pouch extended closest to the ventral commissure of the anus, the other one being 479_{26}. Neither of these two infants was among the earliest stages; one of them (No. 30) was 7.5, the other one 7.8 months intrauterine age.

In Figure 13 (479_{28}, 1943) a similar sketch is presented of the pelvis of a female infant in which the rectovaginal pouch extended farther caudally than in any of the other female infants recorded in Table IV; again it was not one of the youngest female infants (8.1 months' intrauterine age as against 6 months in the youngest infant).

The variation of the value expressing distance of the bottom of the rectogenital pouch from the anus, is very considerable, and since as mentioned (Tables I and II) there is also great variability of this value in the adult, it is very difficult to feel certain as to the significance of these variations in the infant. Attention should be called, however, to the fact, that in a general way the pouch of both sexes extended farther caudally in infants born one or several months before term than in those which were born close to or at term.

Fig. 7. Pelvis of a female infant (dissection 48, 1936), colored, born at term, seen in a dorsal view, after the sacrum, coccyx and rectum had been removed. The dorsal wall of the vagina, incised longitudinally, is seen; it is covered in its full length with peritoneum. The rectovaginal pouch extended fully to the floor of the pelvis.

But there is another line of evidence which suggests rather forcefully that a retraction of the rectogenital pouch in both sexes does take

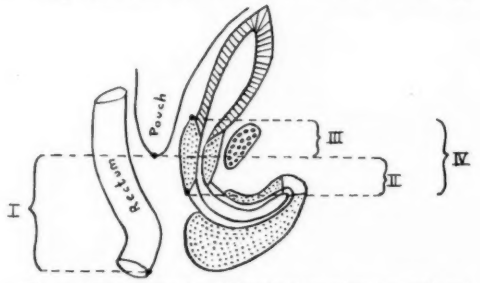

Fig. 8. Diagrammatic midsagittal section through pelvis of male infant, showing landmarks which were used in four routine measurements. *I*, Distance of bottom of rectovesical pouch, cranial to ventral commissure of anus. *II*, Distance of bottom of rectovesical pouch, cranial to apex of prostate gland. *III*, Distance of bottom of rectovesical pouch, caudal to base of prostate gland. *IV*, Length of dorsal surface of prostate gland.

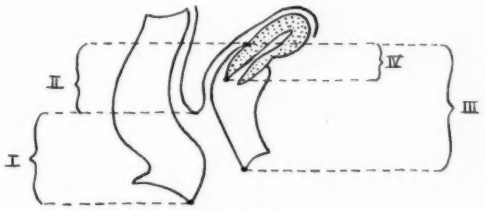

Fig. 9. Diagrammatic midsagittal section through pelvis of female infant, showing landmarks which were used in four routine measurements. *I*, Distance of bottom of rectovaginal pouch, cranial to ventral commissure of anus. *II*, Distance of bottom of rectovaginal pouch, caudal to dorsal fornix of vagina. *III*, Distance between dorsal fornix of vagina and dorsal commissure of opening of vagina (length of vagina). *IV*, Distance between dorsal fornix of vagina and external orifice of cervix (length of intravaginal portion of cervix).

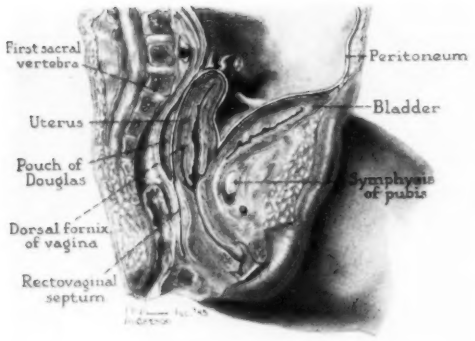

Fig. 10. Left half of pelvis of negro female infant (4704, 1943), born at term, as it appeared in medial view. Showing the rectovaginal septum. For measurements see Table II.

place, at least in some cases, even after birth. As has been stated, in the adult male the rectovesical pouch extends rarely below the level of the cranial end of the prostate gland, and in the adult female only a narrow strip along the cranial end of the dorsal vaginal wall is covered with peritoneum.

But in infants ranging from 6 months intrauterine age to full term (Tables III and IV), large portions of both prostate gland and dorsal vaginal wall may be covered by the peritoneum of the rectogenital pouch. In the male infants the bottom of the rectovesical pouch was located only in a single case cranial to the base of the prostate gland, and this was one of the older infants (8.5 months of intrauterine age). In the other 19 cases the pouch

TABLE III.—DEPTH OF RECTOVESICAL POUCH IN MALE INFANTS (in mm.)

Series 4791-36, 1943

(For method of measurement see Fig. 8)

Number	Pregnancy in months	Crown-rump length in cm.	I Bottom of pouch to anus (ventral commissure)	II Bottom of pouch to lower end of prostate	III Distance of prostate covered by peritoneum	
					a. In mm.	b. In per cent of total length of prostate
20	6.5	22.0	17.0	7.5	6.0	75
11	6.5	22.0	20.0	12.0	5.0	50
22	6.6	23.0	17.0	8.0	8.5	74
24	6.8	23.5	14.0	6.0	10.0*	100+
17	7.0	24.5	18.0	12.0	5.0	56
25	7.0	24.5	16.0	6.0	8.0	67
31	7.0	24.0	19.0	10.0	2.0	21
35	7.0	24.5	21.0	8.0	8.0	73
27	7.2	25.0	24.0	11.5	3.0	60
14	7.2	25.0	18.3	10.2	6.0	67
19	7.3	25.4	21.5	8.0	8.0	73
13	7.5	26.5	19.5	9.6	6.0	67
18	7.5	26.3	20.0	11.0	..	..
30	7.5	26.0	13.0	−2.0	12*	100+
26	7.8	26.5	13.0	7.0	12.5*	100+
29	7.8	27.2	22.0	11.0	12.0	86
36	8.0	28.0	27.0	12.0	5.0	38
10	8.5	29.0	20.1	12.0	11.0	79
16	8.5	29.5	31.0	21.0	−1.0‡	0−
34	9.0	31.0	25.0	7.0	3.0	15

*Bottom of pouch lies below prostate.
‡Bottom of pouch lies above prostate.

Fig. 11. Left half of the pelvis of male infant (479_{26}, 1943) of 7.8 months intrauterine age. Rectovesical pouch descends as far caudal as to the level of caudal end of prostate gland. Instead of a rectovesical septum, a hollow spur projects caudally from the ventral wall of rectovesical pouch. For measurements see Table I. *A*, Rectovesical pouch; *B*, peritoneum; *C*, intestinal canal; *D*, longitudinal musculature of rectum; *E*, internal sphincter of anus; *F*, external anal sphincter; *G*, bladder; *H*, prostate gland; *I*, pubococcygeus muscle; *K*, central perineal body; *L*, symphysis pubis; *M*, bulb of urethra; *N*, bulbocavernosus muscle.

extended caudally to a level corresponding to 15—100 per cent of total length of dorsal surface of the prostate gland; in 3 of these cases the bottom of the rectovesical pouch was located even caudal to the lower end of the prostate gland. In the 16 female infants recorded in Table IV, 19—57 per cent of total length of dorsal vaginal wall was covered with peritoneum and in 1 female infant illustrated in Figure 7 the entire length of the vagina was covered with the peritoneum of the ventral wall of the rectovaginal pouch.

Moreover the measurements suggest that during late intrauterine life the process of fusion of the dorsal with the ventral wall of the rectovaginal pouch is constantly in progress. In the male infants the average distance of the prostate, covered with peritoneum at the intrauterine ages from 6.5 to 7.8 months, was 71 per cent of the total length of the prostate, while in male infants ranging from 8 months to full term only 33 per cent of the total length of the prostate was covered with peritoneum. This means that during the last month of pregnancy the rectovesical pouch receded far over half the distance of the prostate gland, which it covered during the preceding 1½ months.

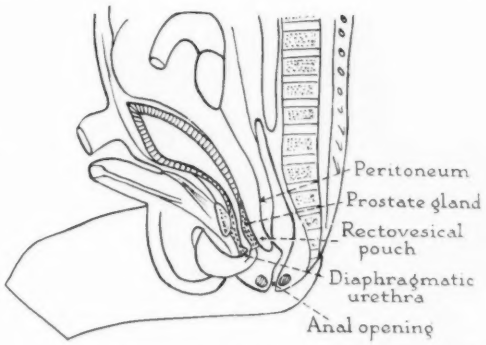

Fig. 12. Diagrammatic midsagittal section through pelvis of a male infant (479_{30}, 1943) of 7.5 months' intrauterine age. The bottom of the rectovesical pouch extended caudally 2 millimeters below the apex of the prostate gland. The entire dorsal surface of prostate gland was covered by peritoneum.

In the female this process of retraction is not so pronounced. In infants ranging from 6 to 7.8 months intrauterine age the cranial 32 per cent of the vagina is covered with peritoneum, while in infants ranging from 8.1 months to full term the part of the dorsal vaginal wall covered by peritoneum amounted to 29 per cent of the total length of the vagina. For some unknown reason the progress of retraction in the female is retarded at an earlier age than in the male infant, resulting in the well known fact that in adult females the bot-

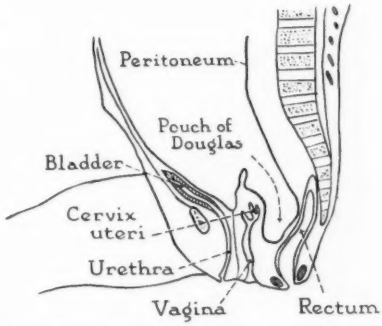

Fig. 13. Diagrammatic midsagittal section through pelvis of a female infant (479_{28}, 1943) of 8.1 months of intrauterine age. The bottom of the rectovaginal pouch lies far below the level of the external orifice of cervix; 39 per cent of the total length of the vagina is covered with peritoneum.

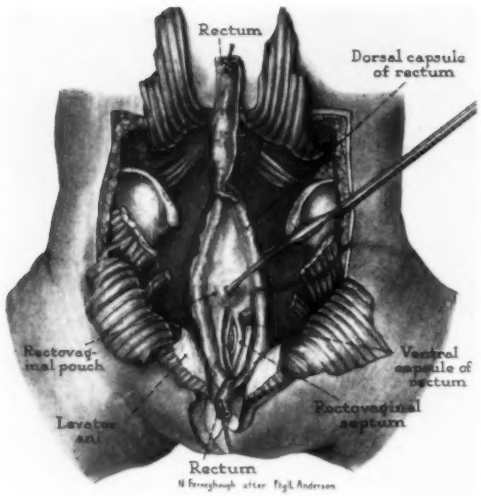

Fig. 14. Dorsal dissection of a negro female infant (479₂, 1943) born at term. The fascial capsules of the rectum and vagina, and the rectovaginal septum are shown as independent structures. The dorsal capsule of rectum was slit open longitudinally and reflected. The rectum was cut through transversely and its stumps reflected. The ventral capsule of rectum was slit open and retracted laterally; on the left side it was left attached to the bottom of the rectovaginal pouch, on the right side its cranial end was separated from peritoneum of rectovaginal pouch and reflected caudally. The rectovaginal septum is seen in the space between retracted parts of ventral capsule of rectum; in the slit of the incised septum is seen the dorsal capsule of vagina and through a slit in it the muscle layer of the dorsal wall of the vagina.

tom of the pouch in general lies closer to the pelvic floor than in adult males.

In the female infant (among other infants) illustrated in Figure 10, the rectovaginal septum was carefully examined and dissected in its median portion; for a distance of 27 millimeters of its longitudinal extent it could be clearly displayed. Its cranial end was firmly attached to the bottom of the rectovaginal pouch into the peritoneum of which it continued without any perceptible boundaries. The most caudal portion of the septum (beyond the extent of 27 mm.) could not be clearly displayed; it seemed to broaden out (in dorsoventral direction) due to the inclusion of fibrous tissue, both ventrally and dorsally; some of the fibers seemed to be muscle fibers. The septum was anchored, by this thickened portion, into the pelvic floor just cranial to the sphincter ani externus. By gentle pressure, with a flat and blunt instrument, against the bottom of the rectovaginal pouch, the septum could easily be separated into a dorsal and a ventral leaf, corresponding to the fused walls of the pouch.

One feature which is most conspicuous in the adult could be clearly demonstrated already in these early stages. In both sexes there is only some loose cellular tissue located in the space between the rectum and the rectogenital septum. Ventrally, on the contrary, the septum is closely adherent to the prostate gland in the male infants and to the dorsal wall of the vagina in the female infants.

In Figure 14 a dorsal dissection of the pelvis of a female infant (479₂, 1943) is illustrated. The sacrum had been removed, the dorsal fascial capsule of the rectum was split open longitudinally and reflected, the rectum was cut through and its stumps reflected. The ventral capsule of the rectum was carefully incised longitudinally and retracted to either side. The rectovaginal septum was slit open and the capsule on the dorsal wall of the vagina was exposed through the slit of the retracted sides of the septum. The vaginal capsule was then incised and the muscle layer of the dorsal vaginal wall came into view. Throughout the dissection it was quite easy to differentiate between the peritoneum and the fascial components. But it was impossible to distinguish the rectovaginal septum from the peritoneum of the rectovaginal pouch. There was no boundary between the two structures; the transition of the peritoneum of the dorsal wall of the pouch into the septum was imperceptible. By palpation with the fingers, guided by previous experiences, the approximate extent of the pouch was ascertained and an incision was made about 1 centimeter above the level at which the pouch was believed to end. A blunt probe was then inserted through the opening and the caudal boundaries of the pouch were determined, as shown in Figure 14. All these observations were checked and verified by further dissection after the drawing had been made.

As in the specimen illustrated in Figure 7, an attempt was made to reopen the fused

TABLE IV.—DEPTH OF POUCH OF DOUGLAS IN FEMALE INFANTS (in mm.)

Series 4791-26, 1943

(For method of measuring see Fig. 9)

Number	Pregnancy in months	Crown-rump length in cm.	I Bottom of pouch to anus (ventral commissure)	II Posterior fornix to bottom of pouch	
				a.	b.
				In mm.	In per cent of total length of vagina
15	6.0	20.0	20.0	4.0	19
21	6.5	21.0	16.0	9.0	41
5	..	21.0	14.0	6.0	40
6	6.7 (30 wks.)	..	..	6.0	14
33	7.0	24.5	20.0	12.0	57
9	7.0	24.0	26.0	6.0	21
8	7.2	25.0	26.0	10.5	33
23	7.8	27.0	24.0	12.0	34
28	8.1	28.2	11.0	7.0	39
32	8.3	28.5	34.0	7.0	18
12	8.5	29.0	25.5	11.0	38
7	9.0	..	43.0	12.3	25
1*	9.0	..	33.0	14.0	31
2*	9.0	..	33.0	11.0	24
3*	9.0	..	36.0	15.0	34
4	9.0	..	36.0	9.0	20

*Have been measured from a dorsal opening into the pelvic cavity (see special records).

part of the pouch by cautious pressure exerted upon the bottom of the pouch; the line of fusion was easily opened and the septum split into its ventral and dorsal leaves.

Another important observation was made in this specimen. The dorsal capsule of the rectum could be displayed easily along the entire length of the gut. The ventral capsule on the contrary became fused to the dorsal wall of the pouch and could not be displayed farther cranially as a layer independent of the peritoneum. As stated previously, the same situation exists in many adult subjects.

SUMMARY

1. In the subperitoneal space which separates the rectum from the urogenital organs, a transverse membranous septum, the rectovesical septum in the male, the rectovaginal septum in the female, is present which is attached cranially to the peritoneum at the bottom of the rectogenital pouch, and caudally to the dorsal surface of the prostate in the male, to the dorsal surface of the vagina in the female. In some cases it may extend as far caudal as the pelvic floor.

2. Two views concerning the nature of this septum are in existence. According to one of them the septum is the result of a fusion, in earlier intrauterine life, of the dorsal with the ventral wall of the rectogenital pouch which originally extends as far caudal as the pelvic floor. According to the other view the septum is not of peritoneal origin but is purely of fascial origin. There is a third group of investigators who have not been able to demonstrate this septum in the female but claim that the tissue between rectum and vagina consists merely of the fascial capsules of these two organs and some loose "areolar tissue" in between them.

A. Observations in adults. 1. With few exceptions the rectogenital septum can be clearly demonstrated in the adult pelvis of

both men and women, either in midsagittal sections through the pelvis or in dissections of the pelvis from the dorsal side. While there are subjects in which the septum is missing and others in which it is perforated or consists only of separate strips, it represents most often a firm transverse membranous partition between rectum and urogenital organs, attached cranially to the peritoneum of the pouch, caudally to the urogenital organs.

2. In most instances the septum can be demonstrated as an individual structure additional to, and independent of, the fascial capsules of the adjacent viscera.

3. There is, however, a constant difference in the relation of the septum to the capsules of the rectum and urogenital organs. From the capsule of the rectum the septum is separated by ample, yet easily broken down loose areolar tissue, but adheres closely to the capsules of bladder, seminal vesicles, and prostate in the male and to the capsule of the vagina in the female. In creating perineal access to the space between rectum and urogenital organs the septum invariably comes to lie ventral to the finger, separating the finger from the prostate or vagina.

4. When seen from outside or in sagittal sections, the rectogenital septum is continued without any visible boundary into the peritoneum of the rectogenital pouch.

5. Its surface texture is entirely different from that of adjacent fascial membranes. While the latter present a dull, whitish and felt-like surface, the surface of the septum is glistening, evenly membranous, of firm texture and sometimes of faintly greenish color.

6. The peritoneum of the pouch, when inspected on its inner surface, presents along the line along which the septum is attached to its outside, features which make this line most conspicuous as compared to the smooth, even surface of the remainder of the peritoneum of the pouch.

The attachment of the septum is marked by a simple whitish line which resembles a scar and may be slightly grooved. In some cases slight wrinkles running perpendicular to this line, may be seen in the peritoneum on either side of the line. In extreme cases the peritoneum is thrown into marked folds perpendicular to the line and strong peritoneal cords are developed bridging across the line, evidently as safeguards against splitting the septum and reopening the fused part of the pouch. The obvious interpretation of these features is that the white, scar-like line on the inner surface of the peritoneum of the pouch is the line along which the dorsal and ventral wall of the pouch have fused with one another and that in some cases special structures, such as the peritoneal cords, have developed to prevent a reopening of the closed portion of the pouch.

7. In accordance with these views is the fact, that application of cautious pressure along the white line will easily split the septum into its original dorsal and ventral leaves.

B. Observations in infants. 1. With exception of a single female full term infant in which the rectovaginal pouch still extended down to the pelvic floor, in 36 male and female infants, varying from 6 months' intrauterine age to full term, the rectogenital pouch of the peritoneal cavity had already started to retract from out of the rectogenital space and the rectogenital septum was developed.

2. As in adults, the rectogenital septum of infants is clearly differentiated as an individual membranous structure, independent of the fascial capsules of the adjacent pelvic viscera.

3. Relative to the prostate in the male and to the vagina in the female, however, the rectogenital pouch in the infant descends to a more caudal level than it does in adults; therefore larger portions of both prostate and vagina are covered by the peritoneum of ventral wall of pouch in infants than in adults.

4. The extent to which the prostate and vagina are covered by peritoneum diminishes distinctly during the last months of intrauterine life, indicating that further retraction of the pouch is in progress during this period.

5. As in adults the tissue of the rectogenital septum is continued without perceptible boundary into the peritoneum of the rectogenital pouch. When viewed from outside it cannot be distinguished from the peritoneum of the pouch, but is well differentiated from adjacent fascial tissues.

6. Applying slight pressure to the bottom of the rectogenital pouch, one succeeds easily

in splitting the septum into a dorsal and ventral leaf, corresponding to the dorsal and ventral walls of the pouch, through fusion of which with one another the septum has formed during earlier stages of development.

CONCLUSIONS

Considering all the evidence presented in this article the authors conclude that the rectogenital septum, as shown for the first time by Cuneo and Veau, is of peritoneal origin and the result of a fusion of the dorsal with the ventral wall of the rectogenital pouch.

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THE EFFECT OF SURGICAL INTERRUPTION OF THE GASTRIC BLOOD FLOW UPON GASTRIC SECRETION AND THE PREVENTION OF EXPERIMENTAL PEPTIC ULCERS

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CONSIDERATION of energy metabolism of the secreting parotid gland has shown that active secretion utilizes oxygen and glucose, that the secretory pressure attains heights greater than the blood pressure indicating that the secretion is not simply an ultra filtrate of plasma, that augmentation of vascularity occurs concomitantly with secretion. It has been known for some time that an increase in vascularity is a prerequisite for glandular secretion (11).

Gray has computed the energy requirement for 1,000 cubic centimeters of active gastric parietal cell secretion to be about 1.5 calories which could be furnished by the oxidation of 5 grams of glucose. If 25 milligrams of glucose were removed from every 100 cubic centimeters of blood, 168 cubic centimeters of blood per minute would have to circulate through the stomach to sustain a parietal secretion of 1,000 cubic centimeters per hour. Richards and coworkers have demonstrated a marked increase in the vascularity of the stomach during active secretion; others have found an increase of 30 to 40 per cent in cardiac output during active digestion. The energy requirements for active gastric secretion are satisfied by additional gastric blood flow.

Somervell employed ligation of gastric vessels as a mode of therapy in patients with peptic ulcer. He demonstrated reduction in free hydrochloric acid output following these ligations. The experiments of Layne and Bergh on dogs seemingly invalidate these clinical claims. Their animals did not survive ligation of all the major gastric vessels and ligations of lesser magnitude effected no change in the acidity of histamine stimulated gastric juice.

Hay and associates have shown that injection of histamine in beeswax is productive of typical peptic ulcers in laboratory animals. Lannin has used histamine in beeswax to test the value of various types of gastrectomies in dogs. The failure to develop peptic ulcers after histamine in beeswax injections would critically test the value of gastric artery ligation as a form of therapy for peptic ulcer. As yet, there has been no adequate experimental confirmation to indicate that the utilization of the ligation procedure would produce worthwhile results.

EXPERIMENTAL

The major gastric arteries of dogs were ligated under general anesthesia. The left and right gastroepiploic arteries and vasa brevia were ligated and divided. The right gastric vessel is small and inconstant in the dog, but when it could be identified it was likewise ligated.

The surviving dogs were kept for periods of 1½ to 3 months and then given daily intramuscular injections of 30 milligrams of histamine in beeswax. The dogs were sacrificed on the 15th day. Normal dogs were used as control animals for the histamine in beeswax injections.

The gastric secretory responses were studied with regard to volume and acidity in 4 dogs surviving 1½ months or longer.

RESULTS

Thirty dogs were subjected to gastric ligations. Of this group, 16 died before injections of histamine and beeswax were started. In these 16 dogs, the stomach showed a diffuse area

From the Department of Surgery, New York University College of Medicine, done on a grant from the U.S. Public Health Service, National Institute of Health.

TABLE I.—GASTRIC SECRETORY STUDIES ON FOUR DOGS SURVIVING GASTRIC VESSEL LIGATION

Dog No.	Before ligation								After ligation							
	Fasting				Post histamine				Fasting				Post histamine			
	pH	Free acid	Total acid	Volume in c.c.	pH	Free acid	Total acid	Volume in c.c.	pH	Free acid	Total acid	Volume in c.c.	pH	Free acid	Total acid	Volume in c.c.
349	7*	0	QNS	2	1.7	92	100	83	7*	0	QNS	2	1.8†‡	72†‡	84†‡	15†‡
416	7*	0	QNS	2	1.2†	104†	111†	125†	7*	0	QNS	2	1.3†‡	96†‡	106†‡	25†‡
440	7*	0	QNS	2	1.1	112	119	130	7*	0	QNS	2	1.1	117	121	40
1 LE	7*	0	QNS	2	1.9	70	77	71	7*	0	QNS	2	2.1†‡	53†‡	68†‡	7†‡

*Approximate value as determined by test papers.
†On occasion (not included in the average) no free acid was obtained and pH was in region of 4.0.
‡On occasion (not included in the average) no juice was obtained and stomach washings with distilled water contained no free acid.

of infection in 4. In 4 others, perforated ulcers were seen on the greater curvature adjacent to the spleen. In 2 dogs a nonperforated gastric ulcer was seen adjacent to the spleen on the greater curvature of the stomach. In 6 dogs the stomach was normal, death being due to other causes.

Fourteen dogs survived a period of 1½ to 3 months; these dogs were injected intramuscularly with 30 milligrams of histamine in beeswax daily for a period of 14 days and sacrificed on the 15th day. Four of these dogs died before completion of the injections. Of these, 2 had large perforated ulcers high on the greater curvature adjacent to the spleen. One dog died of other causes but was found to have a chronic penetrating ulcer in a similar position. The ulcers were similar in appearance, position, and shape to those seen in dogs in which ulcers had developed following vascular ligation alone. One dog had occasional very shallow pinhead sized erosions in the prepyloric area. The remaining 10 dogs were sacrificed on the 15th day and were subjected to postmortem examinations. Of these dogs, one showed occasional pinhead sized superficial erosions in the antrum. The 9 other dogs showed no evidence of ulceration upon examination.

Ten normal control dogs were given daily intramuscular injections of 30 milligrams of histamine in beeswax and were sacrificed on the 15th day. Four dogs had typical duodenal peptic ulcers and 1 dog had a typical prepyloric peptic ulcer on the lesser curvature. Of the remaining 5 dogs, 2 showed small duodenal erosions and 2 showed hemorrhagic duodenitis or gastritis. Although only half of the dogs developed typical peptic ulcers, in none was the stomach or duodenum found to be normal.

In 4 dogs, the secretory responses to aqueous histamine (1 mgm.) were studied in the fasting state before and after ligation. This was accomplished by passing a tube through the mouth into the stomach. The stomach was emptied of its contents by aspiration immediately before the administration of histamine and 1 hour later. The pH of the aspirated contents was obtained by means of a glass electrode. The free and total acids were determined with Topfer's reagent and phenolphthalein. If the fasting contents contained free acid, the test was discontinued and repeated on another day. The average of the 3 most optimum responses of 6 or more tests are tabulated in Table I. As a rule, gastric ligation did not affect the values for pH and free and total acid in the optimum responses, but the volume of secretion was markedly reduced. The results are in accord with those of Layne and Bergh who did not, however, study secretory volume changes. Following ligations, the secretion was so scant that, on many occasions, it was often necessary to wash out the stomach with distilled water in order to determine the presence of free acid. Often histamine failed to evoke a secretory response after ligation, or the juice was low in free acid and of relatively low hydrogen-ion concentration (pH).

The response to insulin was likewise tested and was found to be such a weak stimulus that consistent results were not obtained prior to

ligation. As a rule the free acid rarely rose above 50 units before ligation, and little response was obtained with a comparable dose after ligation.

MICROSCOPIC EXAMINATION OF ULCERS PRODUCED

Those ulcers which appeared in the control dogs (without vascular ligations) were typical peptic ulcers, the description of which is so well known that only brief mention will be made of the changes for purposes of contrast. These ulcers all had sharply demarcated margins with overhanging edges of viable mucosa. As a rule, the following zones could be made out in the ulcer: a zone of necrosis, a zone of fresh granulation infiltrated with inflammatory cells, and a zone of fibroplasia (beginning scar tissue formation) at the base. The viability of the mucosa adjacent to the ulcer was unimpaired.

All the ulcers appearing in those dogs which had ligations of their gastric vessels differed from the true peptic ulcers described. Mucosal coagulation necrosis (or the earlier cellular changes of this process) adjacent to the area of ulceration was always found. In those dogs dying with infarction, the necrosis was more widespread but still more pronounced in the mucosa. The inflammatory reaction and the zone of viable granulation tissue were much less prominent in this group of ulcers and frequently absent. The microscopic findings for the reasons enumerated failed to illustrate a punched out area of ulceration but rather presented an area of superficial necrosis which became deeper as the center of the ulcer was reached.

Briefly, the true peptic ulcers show lytic necrosis produced by digestion of living tissue. The ulcers of vessel ligation show coagulation necrosis with secondary digestion; and the tissue response, which is dependent upon blood supply, is less pronounced.

DISCUSSION

Cutting and associates studied the volume and acidity of gastric secretion in cats together with simultaneous volumetric measurements of venous return from the stomach. They found the volume of acid secretion, after histamine stimulation, to be directly proportional to the rate of blood flow. When the rate of gastric blood flow, after histamine stimulation, was altered by physical means or vasomotor drugs, a corresponding change occurred in the secretory volume. They conclusively proved that with an augmented rate of secretion an increased blood flow occurs, and that any factor which prevents this increase in blood flow will likewise restrict the secretory response. All of our experimental findings are in complete accord with the findings of Cutting and his coworkers.

Whether the ligation of vessels would be a practical method of reducing gastric secretion and whether this reduction would be sufficient to prevent or cure peptic ulcers is a matter of conjecture.

That the human stomach can be almost completely deprived of its blood supply and yet remain viable has been adequately demonstrated in the operative attack on carcinoma of the esophagus. In this procedure, the stomach is drawn into the chest cavity and anastomosed to the distal cut end of the esophagus. The failure to develop vascular ulcers and infarctions in most of the dogs operated upon further illustrates the extent to which the stomach may be deprived of its vascular supply, other reports (8) to the contrary notwithstanding. It became apparent early in the course of the experiment that if the stomach were not handled with extreme gentleness, ulcer or infarction would occur. In the last 12 dogs on which ligations were performed, in not one did infarction or perforated gastric ulcers develop.

It may well be that those dogs operated upon in the histamine treated group which had gastric ulcers had them prior to the injection of histamine in beeswax. Microscopically, the maturity and the density of fibrosis tended to confirm this impression. Also, the ulcers developing from ligation alone were high on the greater curvature adjacent to the spleen. The ulcers which developed after histamine in the ligated group were in an identical position and similar in type. The microscopic pathology previously discussed was characteristic of vascular ulcers and unlike true peptic ulcer. One must therefore conclude that the ulcers devel-

oping in the ligated group were on a vascular basis. In sharp contrast, ulcers developing in the histamine treated controls were typical duodenal and prepyloric peptic ulcers. Ligation of the major gastric vessels had protected against the development of "typical" peptic ulcers, and, in addition, had protected against associated ulcer pathology such as hemorrhagic gastritis or duodenitis and duodenal erosions.

It is possible that the beneficial effects of vagotomy may be produced by a reduction in blood flow caused by section of the vasodilator nerve fibers to the blood vessels of the stomach. Section of the vasoconstrictor or sympathetic nerve fibers to the stomach is frequently productive of typical peptic ulcers (1). A concept of the secretory mechanism, as proposed by Mathews, was that the production of secretion was effected by an increase in blood flow. The autonomic nerves serve as regulators of the blood flow. Such a concept is an oversimplification since it disregards the qualitative changes in secretion resulting from either sympathetic or parasympathetic stimulation. Nevertheless, it seems that the alteration in blood flow which is produced by such nervous stimulation is the factor of major importance. More recently, Wolf has shown that a striking decrease in gastric blood flow takes place after the performance of vagotomy in humans.

That protection by ligation occurs without alteration in the *p*H of the optimum histamine response may seem incongruous. An all or none law for parietal cell secretion has been adequately proved (1). The parietal cell either secretes hydrochloric acid at a fixed acidity or does not secrete at all. Alterations in *p*H and free and combined acid result from partial neutralization of this hydrochloric acid by other alkaline components of secretion (5, 10). Histamine stimulates almost exclusively the acid components of secretion. Since the *p*H of histamine stimulated juice is unchanged by vascular interruption, those cells which are able to secrete do so in the all or none fashion at a fixed *p*H.

However, a reduction in blood flow does not make allowance for the satisfaction of the energy requirements of rapid secretion and the volume of free acid secretion is reduced. This reduction in the total amount of free acid is sufficient to protect against ulceration; the duodenum is able to neutralize small quantities of hydrochloric acid effectively. The importance of the volume of acid pepsin in the production of ulcers has been established in a previous publication (9). It is of importance to point out that, although optimum responses were unchanged qualitatively in the ligated group, the dogs (except No. 440 in Table I) did not respond in more than half of the instances to histamine stimulation and remained achlorhydric or had scant secretion of low acidity. Since these same dogs responded well prior to ligation, one must assume that the ligation was the factor which was responsible for the lack of response.

A reduced gastric blood flow might effectively lower the hydrogen-ion concentration of the total gastric secretion by decreasing the acid component, when the stimulus involves both acid and alkaline components (as in vagus stimulation). The fact that insulin stimulation (post ligation) did not markedly alter the *p*H of the stomach contents may be explainable on this basis.

Postmortem examination of dogs as long as 4 months after ligation of the gastric vessels did not reveal a collateral circulation comparable to the initial circulation. It is therefore reasonable to make the assumption that the effects of such extensive ligations would be permanent.

Peptic ulcer of the esophagus is most often associated with ectopic gastric mucosa, and peptic ulcers are not infrequently found in the stomachs of paraesophageal hernias. Even so, peptic ulcers do not form in the esophagus after the operation which has been described by Phemister, for removal of carcinoma of the esophagus. This fact may be attributable to the reduction of blood flow in the stomach transplanted to the intrathoracic position. Such clinical observation would tend to support the efficacy of gastric ligation as a form of therapy for peptic ulcer.

SUMMARY AND CONCLUSIONS

Ligation of the major gastric vessels by disturbing the energy requirements for secre-

tion can effectively reduce the amount of hydrochloric acid secreted by the stomach. This reduction in acid formation is sufficient to protect dogs from development of typical peptic ulcers induced by the intramuscular injections of histamine in beeswax. With extensive ligations, however, there is danger from the production of vascular ulcers on the midportion of the greater curvature of the stomach. Investigative work is now being carried out to determine the extent of ligation necessary for protection which might be free from hazard of vascular ulcers. There is a possibility that the beneficial effects of vagotomy might be attributable to a reduction in gastric blood flow.

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THE REPAIR OF HERNIA

With Special Application of the Principles Evolved by Bassini, McArthur and McVay

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SINCE man first discovered the nature of groin herniation and conceived the idea of surgical repair, the archives have become replete with procedures and variations, each designed to ameliorate the problem of correcting the anatomic defects and consequent mechanical failure of the supporting structures in that area of the body.

In the selection of a satisfactory herniorrhaphy one must consider certain anatomical, physiological, and mechanical principles that will withstand the scrutiny of statistical studies as pertains to the end-results. These principles, substantiated by experimental observation, seem to be embodied in a combination of the Bassini, the McArthur and the McVay procedures for the repair of hernia. It has seemed to the authors that this can be accomplished by utilizing the locally available aponeurosis of the external oblique as strips of suture material (McArthur) to unite the inguinal structures to Cooper's ligament (McVay) and by reinforcing the floor of the canal (Bassini) as the surgical conjoined tendon is sutured to Poupart's ligament.

THE BASSINI CONTRIBUTION TO HERNIA REPAIR

Eduard Bassini described and illustrated his method of repairing inguinal hernia as he devised it shortly prior to 1890.

The principle of his operation is to reinforce an anatomical defect by decreasing the size of the internal ring and reinforcing the floor of the inguinal ligament. This he did by suturing the three layers, namely, the internal oblique muscle, the transversus abdominis muscle and the "vertical fascia of Cooper" (transversalis fascia) to Poupart's ligament. He then replaced the cord and sutured the fascia of the external oblique over, re-establishing the inguinal canal and the external ring in its normal anatomical position.

Since then many other operations have been designed to narrow the opening at the internal ring and to reinforce the floor of the inguinal canal.

McARTHUR'S CONTRIBUTION TO HERNIA REPAIR

In 1901 L. L. McArthur of Chicago reported the use of strips of the tendinous portion of the external oblique as suture material in performing the Bassini and other popular herniorrhaphies of that time. His technique consisted essentially of splitting the external ring upward and parallel to the fibers of the external oblique as far as the muscle insertion (5 to 6 inches). The edges of the aponeurosis were then raised and a strip of fascia ⅛ to ¼ inch wide was split loose from the internal flap, cut free at the upper lateral end, and left attached at the lower end where the internal pillar of the external ring attaches to the pubic tubercle. If a Bassini type of repair was used, he cut a similar strip from the outer lower flap of the external oblique aponeurosis, ending in the external pillar. These strips were threaded onto a needle and secured with a tie of silk to serve as a continuous stitch. He anchored the end of this stitch by a simple knot or a through and back stitch such as a tailor uses to fix his thread. The cord was placed according to the type of procedure chosen.

McArthur determined the tensile strength of these strips to be between 11 and 24 pounds. He supported his work by dog experimentation in which he showed that the fascia healed *in situ*, was not absorbed, and did not slough. In his final report in 1904 he cited 93 cases without recurrence and 1 example of excised tissue from a man 1 year postoperative showing the fascia strip to be still present.

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If McArthur had lived in this generation he would have, in all probability, applied the use of these fascial strips to a McVay type of repair much as we have done it in accordance with the description outlined in this paper. He suggested that these fascial strips could be used in any type of hernia technique.

The principle of autogenous fascial suture was studied in 1909 by Kirschner. It remained for Gallie and LeMesurier in 1924 to complete the experimental and clinical studies and to establish fascial and aponeurotic suture as a sound, useful, and generally acceptable surgical tool. They demonstrated that a transplant showed the phenomenon of inflammation for a period of 3 weeks, but that no absorption, invasion, or infiltration occurred, and that at the end of 1 year the fascia or aponeurosis had exhibited no histologic change. They concluded that healing between fascial strips and the surrounding tissue occurred by scar formation; that avoidance of intervening areolar tissue and establishment of broad contact surfaces was an aid, but that reliance was placed more upon the suture itself than upon the scar. Gallie and LeMesurier repeatedly demonstrated that their transplanted strips of woven fascia lata had in no instance stretched, contracted, or ruptured.

A transplanted patch of fascia lata was used by Singleton and Stehouwer in the repair of severe direct and ventral hernias. At reoperation of 6 patients they found no reabsorption of the patch. In situations where broad contact between patch and local tissue was impractical they, too, preferred fascia strips since strips did not depend upon scar tissue to maintain the repair. Haas believed that transplanted fascia lata actively participated in a strong union with the muscle to which it was sutured.

In seeking to obviate the necessity of a second operative site, as in the Gallie procedure, Koontz made use of preserved fascia in hernial repair. He found, as did Nageotte, in the case of dead tendon grafts that the preserved fascia became living by a process of repopulation by fibroblasts from the host.

Pedicled grafts of the iliotibial tract of the fascia lata have been employed by Wangensteen for repair of large inguinofemoral and abdominal wall defects. More recently Wangensteen has shifted a patch of fascia from the lower abdomen to cover a defect in the upper abdomen and has then used his pedicle fascia lata graft to cover the dispossessed area in the lower portion of the abdomen. Burton and Ramos made use of the femoral canal through which to conduct a similar pedicle. Mattson devised the use of a flap of rectus sheath to accomplish a Cooper's ligament type of herniorrhaphy.

Neuhof cited 6 to 12 months' follow-up studies of experimental fascial transplants and believed that even autogenous fascial transplants became replaced by a fibrous structure of a nature similar to the original.

In a study of comparative strengths Horsley found fresh autogenous fascia lata to be superior to dead, preserved fascial transplants. Studies which have been made by the aforementioned authors clearly indicate that fascial strips have been widely used, particularly when the defect is so large that the ordinary means of repair seem impractical. When these facts are taken into consideration, one can reasonably conclude, as Payne points out, that fascial suture of the McArthur type should be a very satisfactory suture material to be used in a standard herniorrhaphy.

Burdick and Gillespie summarized the end-results of 1,485 cases in which hernias had been repaired by various types of fascial suture. They felt discouraged with the high incidence of recurrence and infection which was observed with fascial sutures. They made no comparison with groups of hernias of equal severity wherein foreign material was used. Since the highest percentage of the more difficult repairs in their series fell into the fascia group, it seems not justifiable to lay the blame of recurrence on the facial suture.

Guthrie, Olson, and Masson analyzed the results in 2,298 patients and found a recurrence rate of 7.8 per cent with autogenous fascia as against 5.6 per cent for foreign suture material. They found that fascia was used much more frequently in severe and recurrent hernias, obese individuals, those with poor musculofascial development and in men. They felt that by giving reasonable weight to these disadvantages the small statistical difference

could be more than discounted and favor placed with fascial suture.

Gallie believes that failure in many cases of fascial suture repair is due to failure to anchor adequately the end of the strips. A proper tie at the end or a wire retaining suture will prevent slipping.

Burdick and Gillespie feel that the passage of a large needle through Poupart's ligament will cause tearing. Cooper's ligament is sufficiently tough to withstand the strain.

THE McVAY CONTRIBUTION TO HERNIA REPAIR

The use of Cooper's (superior pubic) ligament as an anchor for the inguinal strata has become accepted as a sound surgical procedure since McVay and Anson published their anatomic investigations and suggestions for the surgical application to the repair of inguinal hernia.

Cooper first observed this structure in 1804, and some years later suggested its use in the repair of hernia. Mattson, in reviewing the literature pertinent to Cooper's ligament, stated that Lotheiseen in 1898, and Narath before him, had made use of the superior pubic ligament to repair femoral and inguinal hernias. By 1927 Babcock was using the medial part of Cooper's ligament, near the pubic tubercle, as a part of the procedure in inguinal repair.

Before Cooper's ligament came into general use for inguinal herniorrhaphy Moschcowitz in 1907, Seelig and Tuholske in 1914, and Dickson in 1936 described its use in femoral hernia.

From dissections of over 300 inguinal regions McVay and Anson noted that the inguinal ligament was not the normal insertion for the inguinal portion of the transversalis fascia, transversus abdominis, and internal oblique which are actually inserted on Cooper's ligament and the pubic pecten. They maintain that the relationship of these structures to Poupart's ligament is only one of contiguity.

McVay also stated that the conjoined tendon is an artefact of dissection and that the true falx or ligament of Henle is a lateral expansion of the rectus abdominis tendon of insertion on the pubic pecten. Rienhoff, likewise, found no conjoined tendon as had been previously described. McVay and Anson also observed that the inguinal ligament is only loosely held in its convex position by surrounding fascia and is easily shelled out to become the free margin of the aponeurosis of the external oblique. They demonstrated that when the inguinal strata are sutured to Poupart's ligament a cephalad bending easily occurs which leaves the inguinal region exposed below it. It is their opinion that recurrent hernia masses appear in the stretched, weakened area below the elevated inguinal ligament. It is for these reasons that McVay ignores the inguinal ligament in the procedure of his herniorrhaphy. He sutures, with nonabsorbable material, the inferior margin of the transversus abdominis aponeurosis and its attached transversalis fascia to Cooper's ligament starting at the pubic tubercle and extending along Cooper's ligament to the femoral vein. He states that when the internal oblique muscle is aponeurotic in nature its lower border is also included in the suture.

This bulk of tissue was designated by Bassini as the "dreihaupt;" it has been erroneously called the conjoined tendon and is commonly referred to as the surgical conjoined tendon (Fig. 1).

From observations regarding mechanical forces applied to the inguinal area, Lick and Samson concluded that a hernioplasty which employs Poupart's ligament creates an abnormal trihedral upon which intra-abdominal pressure exerts a force against the hernioplasty wall about sixty-two times that exerted against the normal oblate ellipsoidal floor. They felt that the use of Cooper's, instead of Poupart's ligament, was of great importance because then the normal ellipsoidal contour of the inguinal region was preserved. They also noted that the maximum pressure is only a few millimeters caudad to the deep epigastric vessels at the exact point of appearance of direct inguinal hernia.

A McVay type of repair seems the best mechanical support to this area, providing a barrier against an approach to the floor of the inguinal canal through which direct hernias must protrude in order that they may become evident.

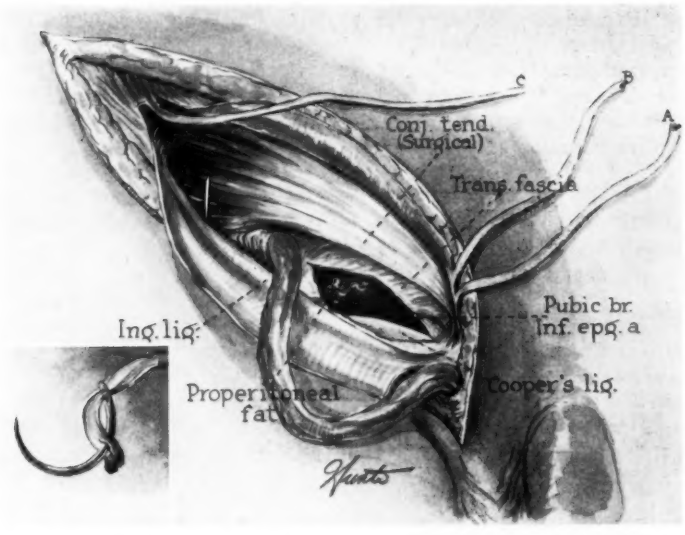

Fig. 1. Fascial strips *A*, *B*, and *C* have been made from the upper leaf of the external oblique aponeurosis. The floor of the inguinal canal has been opened through the transversalis fascia exposing Cooper's ligament which must be dissected free of areolar tissue. The insert shows the method of threading and anchoring a small Gallie type needle.

Harkins and Swenson surveyed their experience with 322 hernias repaired by the McVay type of procedure over a 38 month period ending at the date of writing their report. They had only one recurrence. Many other surgeons have discarded the older type of procedures in favor of the McVay principle.

HERNIA REPAIR COMBINING THESE THREE PRINCIPLES

It has impressed us that each of these principles of hernia repair has some advantages. A procedure has been devised incorporating these principles into the repair of inguinal and femoral hernia.

General anesthesia is employed. Curare is used to obtain relaxation.

The usual skin incision is modified by a slight increase in length and a downward curve in its medial one-third. These variations in the skin incision give a more roomy exposure to the muscular origin of the aponeurosis of the external oblique and the insertion of the fascia in the region of the pubic tubercle and Cooper's ligament.

A broad area of external oblique aponeurosis is dissected free of its areolar tissue. A scissors is inserted into the external ring at the level of its upper margin. The fascia is split from this point laterally to the muscle fibers. This leaves a relatively broad lateral leaf of external oblique fascia which can be dissected from the roof of the inguinal canal and turned back (Fig. 1).

The medial (upper) leaf of this fascia is dissected free from the underlying internal oblique muscle for about 3 centimeters so as to expose the internal oblique muscle and the surgical conjoined tendon.

The hernial sac is dissected free, its base is ligated and Kocherized.

Three ¼ inch strips are then made from the upper leaf of this fascia, precautions being taken to see that the strips do not extend obliquely across the fibers lest tearing develop. The preparation of these strips of fascia constitutes McArthur's contribution to the repair of hernia.

One of these strips is detached from the pubic tubercle end and two from the muscular

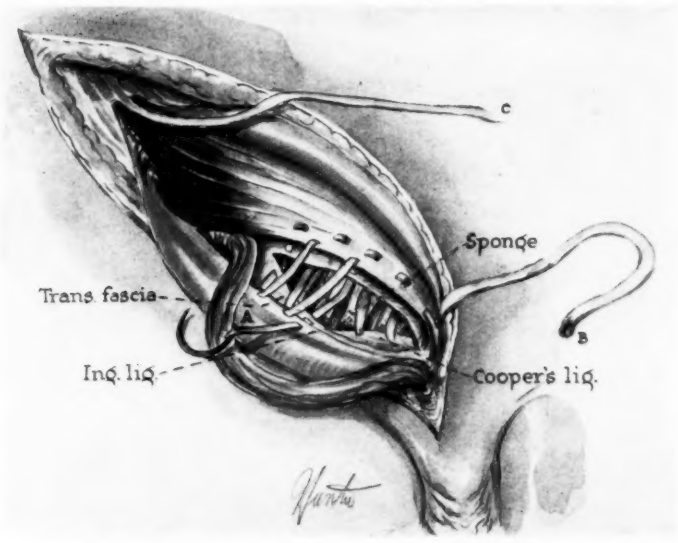

Fig. 2. Fascial suture *A* has been partially completed. By following it from its point of attachment near the pubic tubercle, it will be observed anchoring the surgical conjoined tendon to Cooper's ligament; then passing across the floor of the inguinal canal, reapproximating the transversalis fascia and also approximating the edge of the internal oblique muscle to the inguinal ligament. A sponge holds back the properitoneal fat while this suturing is being made and is removed at this stage of the operation before snugging up the tissues as illustrated in Figure 3.

end, leaving them attached at their opposite ends (Fig. 1, *A*, *B*, *C*).

In order to facilitate anchorage of the strip on a small oval calibered Gallie type needle, the two lateral ends, when cut free, are left with a ⅛ inch bud of muscle attached. The strip with a free medial end is cut transversely so that it contains some cross striations of the reflected portion of the rectus sheath. The fascia strip is inserted through the eye of a Gallie type needle. This strip is then pulled through the eye so that the needle point can be passed through the fibers of the strip about 3 or 4 millimeters from its free end (see insert, Fig. 1). The cross fibers in the muscle bud of the two free lateral ends (Fig. 1, *A*, *B*) and the cross fibers of the free medial end (Fig. 1, *C*) serve to keep the fascia from stripping off the needle when tension is applied while suturing. This threading of the needle also permits use of the full length of the fascia strips.

Cooper's (superior pubic) ligament is now exposed by cutting through the thin transversalis fascia which lies under the cord forming the floor of the inguinal canal (see Fig. 1). If the hernia is direct in character, this has been already accomplished when the sac was dissected out. Usually the pubic branch of the inferior epigastric (or sometimes spermatic artery) passes transversely across the floor of the canal, lying in the deeper structures of the transversalis fascia. This vessel (Fig. 1) must be isolated and tied lest annoying bleeding confuse the further dissection.

Cooper's ligament lies underneath the transversalis fascia and can be easily palpated as a hard tendinous structure. It passes obliquely downward and laterally from the pubic tubercle. This strong, tendinous ligament is exposed laterally, nearly to the femoral vein. A dry 2 by 2 sponge is inserted into this depth to rid the field of properitoneal fat, for protection of the femoral vein and to dissect the loose areolar tissue away from Cooper's ligament. It is left there until the stitches through Cooper's ligament have been placed. It is re-

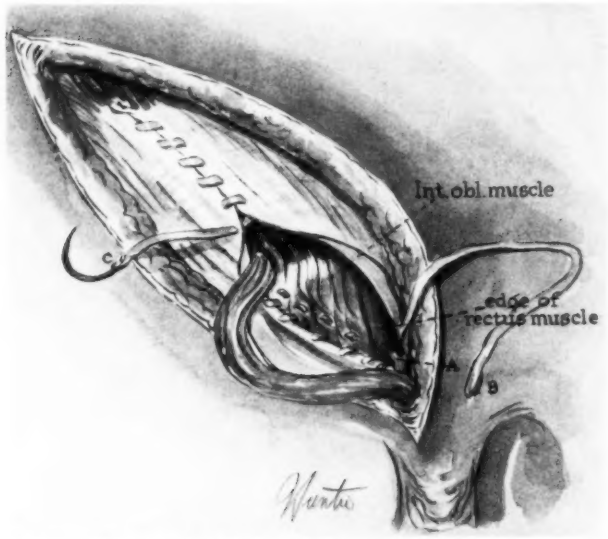

Fig. 3. The internal oblique muscle has been snugged up to Cooper's ligament producing a slight indentation at that point. The edge of the surgical conjoined tendon has been approximated to the inguinal ligament. The internal ring has been completed. Stitch *C* has been partly completed, closing the lateral rent in the external oblique aponeurosis.

moved when this continuous stitch of fascia is pulled taut as this portion of the abdominal wall is approximated to Cooper's ligament (Fig. 3).

In making this exposure of Cooper's ligament, it is important to remember that approximately 20 per cent of individuals disclose an anomalous obturator artery passing perpendicularly across Cooper's ligament as a branch of the inferior epigastric artery. This anomalous artery is either ligated and pushed away from Cooper's ligament or it is scrupulously avoided. It has been justifiably dubbed the corona mortis.

After Cooper's ligament has been adequately exposed, the first strip of fascia, with its attached end at the pubic tubercle, is used to approximate the bundle of tissue commonly called the surgical conjoined tendon to Cooper's ligament (Fig. 2, *A*).

This stitch passed through the bundle of tissue in which lie medially the edge of the rectus sheath (Henle's ligament) and more laterally the bundle of tissue in which lie the internal oblique muscle, the transversus abdominis muscle and the transversalis fascia. It is passed directly through these structures from anterior to posterior, beginning near the pubic tubercle. It then picks up Cooper's ligament and returns through this bundle of tissue from posterior to anterior. In this manner it passes back and forth, weaving a sort of picket fence between Cooper's ligament and this bundle of tissue described by Bassini as the "dreihaupt." Usually three such stitches through Cooper's ligament are sufficient to block the approach to the floor of the inguinal canal and the femoral ring. Four stitches through Cooper's ligament are illustrated in Figure 2.

These stitches are so placed as to leave about ½ inch free margin of the surgical conjoined tendon (internal oblique muscle and transversus abdominis muscle) lying free at the medial margin of the inguinal canal. This free edge of the surgical conjoined tendon is then sutured to the shelving edge of Poupart's ligament with the remaining portion of the fascia strip as the suturing progresses back again toward the pubic tubercle (Fig. 2, *A*)

Fig. 4. Strip *A* now disappears from view. Strip *C* has been completed. Strip *B* has reformed a new external ring and is closing medial end of external oblique aponeurosis.

Fig. 5. All fascial strips have been completed. *B* and *C* overlap for about 2 inches. Each has been anchored with a wire stitch of No. 32 stainless steel.

The internal ring is made smaller by passing the fascial strip close to its medial margin.

The tissues which have been included in this first stitch of fascia (Fig. 2, *A*) are approximated as the fascial strip is snugged up and the end of the fascia strip is anchored with one tie of No. 32 stainless steel wire (Fig. 3, *A*). It is then cut free from the needle. This portion of the procedure completes the first two stages—that of blocking the approach to the floor of the canal by suturing the bundle of muscles and transversalis fascia to Cooper's ligament (McVay), and of suturing the edge of the surgical conjoined tendon to the inguinal ligament thereby reinforcing the floor of the canal (Bassini).

The retracted cord is then replaced into the inguinal canal over its reinforced floor and the edges of the aponeurosis of the external oblique are sutured together over the cord with the second and third running stitch of fascia (Fig. 3, *C* and Fig. 4, *B*)

This changes, slightly, the position of the spermatic cord in that it assumes a slightly higher position as the lateral leaf of the external oblique fascia is pulled over to meet the remaining medial leaf. This also changes the position of the external ring so that instead of finding the pubic tubercle at its medial margin, it now is found at its medial and inferior margin.

Care is taken to stagger the bite of the stitch through the fascia and inguinal ligament in order to prevent splitting of the aponeurosis.

The strip of fascia with its attachment remaining at the muscular end is used to close the lateral rent in the fascia of the external oblique (Fig. 4, *C*). The second and third strips of fascia overlap one another for a distance of about 2 inches (Fig. 5). The end of each strip of fascia is anchored with a wire stitch. No other foreign suture material is used.

Curare is used to promote relaxation of the muscles in order to facilitate approximation without tension.

Bleeding is adequately controlled throughout the course of the operation. The skin is closed with clips.

All patients are fitted with a wide, supporting abdominal girdle which they are required to wear for 6 months after the operation. This is done as a precautionary protection against the breaking of structures during the period in which scar tissue becomes well organized and firm.

SUMMARY AND CONCLUSIONS

The use of fascia as a suture material in a standard inguinal herniorrhaphy is a sound and practical procedure. Evidence, as indicated in the literature, suggests that fascia sutures possess strength in themselves as well as approximating values during the period of fibrous tissue proliferation. The McArthur type of strip has the additional value of being indigenous to the area of repair.

Supporting evidence has been presented, from a review of the literature, showing that the use of Cooper's ligament is anatomically and mechanically correct.

A procedure has been described which employs three generally accepted principles in the repair of hernia, namely, the use of locally available fascia for suture (McArthur) to approximate the inguinal strata to Cooper's ligament (McVay) and the reinforcement of the floor of the inguinal canal (Bassini).

Rather than reserve a stronger type of repair for the recurrent hernias, it seems justifiable to employ the strongest type of repair on the first occasion, thereby eliminating the need for additional repair.

At the date of this writing we have repaired 40 hernias (inguinal and femoral) by this method without complications. There have been no failures, though it is yet too early (6 months) to determine the eventual end-results.

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REDUNDANT BLIND SEGMENTS OF INTESTINE FOLLOWING SIDE-TO-SIDE ANASTOMOSIS WITH DIVISION OF THE BOWEL

Report of 5 Cases

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AFTER the removal of a segment of bowel, several methods of restoring continuity of the intestinal tract are available. Each method has many advocates, and circumstances, such as the anatomic characteristics of the particular segment of bowel involved or the presence of obstruction, may influence greatly the choice of method. The use of a side-to-side anastomosis after the inversion of the two cut ends is a standard, safe method; however, the possibility of complications arising from the proximal end has long been recognized. These complications are almost invariably associated with excessive length of the proximal segment of the bowel distal to the anastomosis and they should be largely preventable by careful attention to the length of this segment. How frequently such complications develop cannot be estimated, but in view of the widespread knowledge of the hazards associated with a redundant segment, we were amazed to find in the literature so few papers dealing with these complications.

Pearse, using dogs, showed that a blind loop of bowel distal to an anastomosis became a functionless segment of intestine if the direction of the peristalsis was away from the blind end and toward the anastomosis. However, if peristalsis was toward the blind end, material was carried into it and stagnated there. The occurrence of changes in the blind proximal loops depended on the length of the loops; in those loops which were less than 2 feet (60 cm.) in length no pathologic changes developed. Those loops 3 to 4 feet (90 to 120 cm.) in length became hugely dilated, hypertrophied, and filled with inspissated intestinal contents. If perforation did not occur, these long blind loops caused anorexia, lethargy, emaciation, and finally death after 3 or 4 months. Excision of the blind loops, if carried out in time, was followed by complete recovery of the animals. Loops 5 to 6 feet (150 to 180 cm.) in length represented such a large part of the total intestinal length that the majority of the animals died from inanition. Estes and Holm, also using dogs, confirmed the observations of Pearse that when peristalsis was toward the blind end of the bowel, after division of the bowel and side-to-side anastomosis either between the ileum and colon or between segments of the small bowel, the blind segments became dilated to three or four times their normal diameter. Ulcers developed frequently and subsequent perforation was not uncommon.

There are few reports of clinical cases in the literature. This may be explained, in part, by the fact that in the past the mortality rate associated with this type of surgery has been high, particularly so in cases in which the technical aspects of the operation were not entirely satisfactory. A fact of greater importance, however, is that probably excessively long loops are not left usually and that shorter loops are not associated with symptoms of sufficient severity to warrant operation. Thus, the statement is made by Rankin, Bargen, and Buie that hypertrophy and elongation of blind loops of ileum have been observed at necropsy years after resection of the colon with side-to-side anastomosis between the colon and small bowel (Fig. 1). Similarly, Pickhardt reported a case of resection of the right portion of the colon and terminal part of the ileum with side-to-side anastomosis between the transverse colon and ileum in which

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the blind loop of ileum became elongated and dilated without causing symptoms. He pointed, out, however, that the blind loop was a potential source of danger from the standpoint of obstruction.

We were able to find reports of a few cases, however, in which serious symptoms were produced by redundant blind loops. Turner referred to a case in which a blind ileal segment, left after resection of the right portion of the colon with side-to-side anastomosis between the transverse colon and ileum, ruptured when the patient fell downstairs. Eckel and Holman reported a case in which vague intermittent abdominal distress developed and persisted, without change, for 10 years after hemicolectomy on the right with side-to-side ileocolostomy. At subsequent operation, a distended, blind segment of ileum distal to the anastomosis was excised with complete cure of the patient. Sletten, in a discussion of Pickhardt's paper, mentioned a case in which such a blind loop perforated. Estes and Holm reported the case of a 16 year old boy in whom, after resection of the terminal part of the ileum and establishment of a side-to-side anastomosis between the ascending colon and ileum, a short blind loop of ileum had been left distal to the anastomosis. A few months later intermittent pain, borborygmi, and low abdominal distention developed. The blind segment had become hugely elongated, distended and ulcerated, and filled almost a third of the abdomen. Resection of the blind loop resulted in complete relief of symptoms. Ginzburg, Colp, and Sussman reported 3 cases in which blind loops of ileum gave rise to symptoms after side-to-side ileocolostomy with division of the bowel. In 2 of the cases the blind ends had been demonstrated clinically, one by roentgen rays and the other by the palpation of a large, sausage-shaped mass. In the third case ulceration had developed in the blind loop and the patient had symptoms of obstruction. In all 3 cases cures followed excision of the blind redundant loops.

A search of the files of the Mayo Clinic revealed records of only 5 cases in which symptoms could be definitely attributed to blind segments of small bowel left after division of the bowel and side-to-side anastomosis between either the colon and small bowel or segments of small bowel. These 5 cases were selected from a larger number in which symptoms, usually suggestive of partial intestinal obstruction, and a redundant segment of bowel beyond the side-to-side anastomosis were noted. However, in each of the excluded cases some other more probable explanation for the symptoms was found. In some cases a recurrence of the original disease, usually regional enteritis, had developed; in others, the segments of the bowel which had been used for the anastomosis were bound down by adhesions or the anastomosis was greatly distorted. Finally, some cases were excluded because of a malfunctioning stoma. It is possible that in some of the excluded cases the blind segment of bowel distal to the anastomosis was the underlying etiologic factor. However, the findings, in such cases, at the time of the subsequent operation were so complex that the symptoms could not be attributed solely to the blind loops. Since we were primarily interested in the syndrome associated with the blind segments alone, it was thought desirable to exclude all such complicated cases.

REPORT OF CASES

CASE 1. A white woman, aged 37 years, was first seen in August, 1942. She complained, chiefly of crampy pains and a mass in the right lower quadrant both of which had been present for 4 years. A diagnosis of regional enteritis was established. Resection of the terminal part of the ileum, hemicolectomy on the right and side-to-side ileocolostomy were carried out. A soft rubber drain, brought out through a stab wound in the right flank, was left in the region of the anastomosis. The patient was dismissed after an uneventful convalescence. She returned 6 weeks later because gas and feces were passing from the site of the previous drain. Gas had first passed from the stab wound about 1 month after the operation, and shortly afterward, fecal material had begun to exude from the sinus. Crampy pain had been experienced intermittently in the right lower quadrant which was relieved by the expulsion of gas either through the rectum or through the draining sinus.

There was no systemic evidence of infection at the time of admission. The incision was well healed but feces and gas exuded from the fistulous tract at the site of the previous drain. A small abscess had developed in the right groin. The leucocytes numbered 17,800 per cubic millimeter of blood. Roentgenographic examination of the colon revealed a freely functioning anastomosis between the colon and

ileum. Nothing further was advised at that time since the sinus closed spontaneously. Two weeks later, however, fecal and purulent drainage again developed, associated with marked constitutional symptoms and fever as high as 103 degrees F. Recovery from this attack was slow and after approximately 10 weeks, surgical exploration of the anastomosis was carried out. The side-to-side anastomosis between the ileum and transverse colon was found to be functioning satisfactorily. There was a redundant blind segment of ileum distal to the anastomosis, the lumen of which connected with the cutaneous opening. This loop of ileum had become hypertrophied and elongated. Ulceration had presumably occurred which had progressed to perforation. The operation was limited to excision of the redundant loop. The patient made an uneventful recovery and has remained well since.

CASE 2. A white man, aged 48 years, was seen in an emergency in July, 1944. He had been awakened in the early morning by severe crampy, abdominal pain which had gradually become worse. There was no accompanying vomiting but some nausea. One year previously, repair of a left inguinal hernia had been carried out at the clinic. Ten days later mesenteric thrombosis had developed, necessitating resection of approximately 28 centimeters of jejunum because of gangrene. Intestinal continuity had been re-established by means of side-to-side jejunojejunostomy.

On admission the patient's temperature was 100.4 degrees F., the pulse was 90 beats per minute and the blood pressure 120 millimeters of mercury systolic and 95 diastolic. The heart and lungs were normal. The abdomen was rigid and tender generally, but tenderness in the right lower quadrant was most marked. Examination of the urine gave negative results. The leucocytes numbered 9,900 per cubic millimeter of blood. A scout film of the abdomen made without administration of barium revealed free gas in the peritoneal cavity.

Surgical exploration was carried out shortly after admission. The blind, inverted end of the proximal segment of jejunum distal to the anastomosis was reddened, thickened, and covered with fibrinous, purulent exudate. The mesentery was thickened and edematous but there was no evidence of mesenteric thrombosis. When the region of the anastomosis was first approached, about 30 cubic centimeters of thick pus was encountered. The blind end of the distal segment of the jejunum was 4 to 5 centimeters in length and showed no evidence of obstruction or inflammation. Both blind ends of bowel were excised and the ends reinverted so that no redundant segments were left. Pathologic examination of the proximal loop revealed inflammation with ulceration, abscess formation and perforation. The shorter distal loop revealed only mild inflammation.

Pneumonia developed postoperatively and, in spite of treatment with penicillin and the sulfonamides, the patient died 8 days after operation.

CASE 3. A white married woman, aged 27 years, first seen in August, 1944, complained of intermittent attacks of crampy abdominal pain, vomiting, di ention, and constipation which had first developed after a partial resection of the small bowel 4 years before. The individual attacks often lasted as long as 4 days. In April, 1940, the patient had undergone surgical exploration elsewhere and appendectomy, left salpingectomy, and suspension of the uterus had been carried out; in September, 1940, 65 centimeters of gangrenous ileum had been excised and a side-to-side anastomosis established between the segments of ileum.

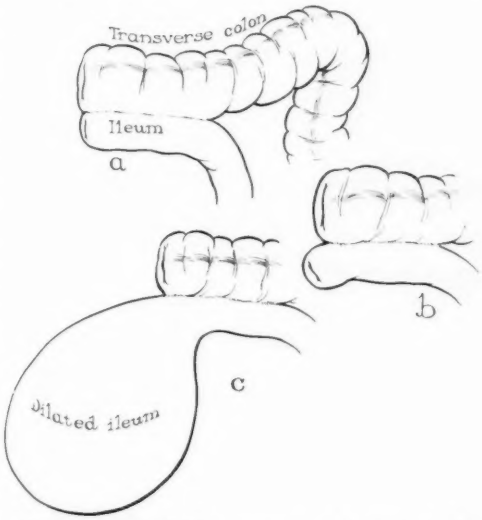

Fig. 1. Side-to-side ileotransverse colostomy. a, Correct method, making united ends of bowel as short as possible; b, slight dilation of proximal end of small bowel which normally occurs; c, large dilated blind loop of small bowel which occurs when redundant loop is left too long.

Physical examination gave essentially negative results except for a ventral hernia which had developed in the scar of the former incision. There were no masses on pelvic examination. Leucocyte and erythrocyte counts were normal, as was the urinalysis. Roentgenographic examination of the chest, stomach, gall bladder, and colon was negative. Roentgenographic examination of the small bowel revealed a dilated blind loop of ileum near the former anastomosis, which seemed adequate.

Surgical exploration of the abdomen was carried out in September, 1944, and the previously established antiperistaltic side-to-side anastomosis between segments of the ileum examined. The proximal blind end of ileum had become elongated and hypertrophied so that it exceeded the size of a normal stomach, being about 45 centimeters long and approximately 10 centimeters in diameter. Excision of the ileocolic stoma, including both blind ends of bowel, was carried out and intestinal continuity was

re-established by an end-to-end anastomosis between segments of ileum. Patient has remained well since.

CASE 4. A white woman, aged 66 years, was first seen in November, 1944. For 2 years she had had diarrhea and crampy abdominal pain, chiefly localized in the right lower quadrant of the abdomen. For the preceding 7 years, in addition, she had experienced, in the right upper quadrant, attacks of pain of a different type which were characteristic of those associated with cholelithiasis. Abdominal exploration had first been carried out elsewhere in 1942 because of the recurring attacks of pain in the upper right quadrant. At that operation the right portion of the colon and terminal part of the ileum had been resected and intestinal continuity had been re-established by means of side-to-side ileocolostomy. Shortly after that operation the intermittent attacks of crampy abdominal pain, localized in the right lower quadrant, along with diarrhea had first developed.

On physical examination the blood pressure was found to be 215 millimeters of mercury systolic and 110 diastolic. The heart and lungs were normal. The abdomen was moderately tender in the right lower quadrant. Urinalysis, erythrocyte count, and a hemoglobin determination gave normal values. The leucocytes numbered 15,500 per cubic millimeter of blood. Roentgenographic examination of the chest and stomach gave negative results and examination of the colon revealed a normally functioning stoma between the ileum and transverse colon. A cholecystogram disclosed a nonfunctioning gall bladder and cholelithiasis.

At operation the ileocolic stoma which had been made previously was examined and found to be adequate. The inverted end of ileum was hypertrophied and extended for a distance of approximately 15 centimeters beyond the anastomosis. The redundant loop of ileum was excised and the end turned in. The gall bladder was also removed.

The patient returned to the clinic for a check-up in November, 1945. No pain had been experienced since her dismissal. In August, 1946, in response to an inquiry, the patient indicated that she was experiencing some distress in the right lower quadrant.

CASE 5. A white man, aged 31 years, first came to the clinic in September, 1945, complaining of intermittent crampy abdominal pain since May, 1945. In 1939 a diagnosis of regional enteritis had been made elsewhere and in 1941 an abdominal exploration had been carried out. Nothing was done surgically to treat the regional enteritis at that operation. His symptoms became progressively more severe and in 1943 a 2 stage hemicolectomy on the right and side-to-side ileocolostomy had been carried out elsewhere. Symptoms recurred and became so marked that a second resection of the terminal portion of the ileum, including the site of previous ileocolostomy, had been performed in April, 1945. Continuity of the bowel was again re-established by means of side-to-side ileocolostomy. The intermittent crampy pains which caused the patient to come to the clinic had developed about a month later.

Physical examination on admission gave essentially negative results with the exception of slight tenderness in the right lower quadrant of the abdomen. The value for hemoglobin was found to be 10.4 grams per 100 cubic centimeters of blood. The leucocyte count was 4,200 per cubic millimeter of blood and urinalysis gave negative results. Roentgenographic examination of the colon revealed a normally functioning stoma between the ileum and transverse colon and a dilated blind loop of ileum proximal to the anastomosis. In view of the number of operations the patient had undergone and the mildness of the present symptoms, conservative management was advised. The patient returned approximately 6 months later, partly because a further check-up had been advised but chiefly because the attacks of crampy pain had occurred with increasing frequency and had become increasingly severe during the interval. Borborygmi and distention accompanied the attacks at that time. Relief occurred when the gas seemed to pass some obstruction. Roentgenographic examination of the colon again revealed a normally functioning stoma between the ileum and transverse colon and the presence of the dilated blind loop of ileum. A delayed film showed prolonged retention of barium in the blind segment of ileum (Fig. 2).

Exploration was advised and carried out in April, 1946. The redundant segment of ileum was hypertrophied and dilated. The blind loops of ileum and colon along with the site of anastomosis were resected and an end-to-side anastomosis was established between the ileum and transverse colon. The patient made an uneventful recovery, and has since regained his normal weight and has remained well.

COMMENT

In view of the reports of cases in the literature and those in the present series, there can be no doubt that potential hazards, associated with the closed end of the proximal segment of bowel, are inherent in the operation of side-to-side anastomosis after division or resection of the bowel. To produce symptoms in dogs, long segments of bowel must be left beyond the anastomosis, and this fact probably explains why clinical cases are uncommon, in that such gross errors of technique are seldom made. Whether the closed end of the proximal segment has any particular tendency to leak early, postoperatively, and so produce peritonitis, cannot be stated. The findings at necropsy in such cases are often inconclusive because of the extent of the local inflammatory reaction. However, early death from peritonitis following resection and side-to-side anastomosis is unusual unless peritonitis has

become established prior to the operation or unless gross fecal soiling has occurred at the time of operation.

In all clinical cases which have been reported, including those in the present series, some time elapsed between the operation and the development of the complication. When localized infectious processes occurred, ulceration evidently developed first with subsequent perforation of the ulcer. The ulceration alone seemed to produce no definite symptoms, and the first evidence that any complication had developed was produced by the inflammatory process outside of the bowel. Thus, in Case 2 of our series all symptoms were obviously produced by the local peritonitis, in Case 1 the earliest symptoms were those associated with an external fecal fistula and in one of Ginzburg, Colp, and Sussman's cases, an inflammatory mass secondary to ulceration produced obstruction. We have no evidence in our material that the inverted end of the proximal segment ever gave way, and the only case of rupture of a redundant loop that we were able to find in the literature was that reported by Turner, which clearly resulted from trauma.

In all the other cases in the present series, as well as in those we were able to find reported in the literature, a fairly uniform syndrome was noted. The symptoms developed at varying times after operation and were, generally speaking, suggestive of partial intestinal obstruction. When the redundant loop was sufficiently hypertrophied, distention was evident clinically; this occurred in Case 1 of the present series and in a case reported by Estes and Holm. More frequently than not there was no evident distention. All patients with chronic symptoms complained of colic of varying intensity. Diarrhea was associated with the colic in Case 4 of our series and vomiting accompanied the colic and distention in Case 3.

In cases in which perforation and symptoms consequent to peritonitis do not occur, the diagnosis depends on the demonstration of the redundant loop by roentgenography after administration of barium. In cases in which the redundant loop is of clinical significance, it should be demonstrable on roentgenologic examination after barium has been given either as an enema or by mouth (Fig. 2). It is conceivable that the redundant loop could be packed so solidly with inspissated stool or secretion that barium could not enter. However, this is probably an unusual circumstance, and in such cases the redundant loop should be palpable on clinical examination. A note of caution could well be sounded concerning the use of barium by mouth in patients who have undergone previous resections of the bowel and who have since had symptoms suggestive of partial obstruction. The symptoms, in such cases, are far more likely to be due to partial obstruction produced by adhesive bands or an inadequate stoma than to redundant loops, and in such cases barium by mouth may be strongly contraindicated.

Fig. 2. Redundant, dilated blind loop of small bowel, following side-to-side ileocolostomy (Case 5).

Some restraint should be exercised, as well, in attributing the symptoms to a redundant segment which may be demonstrated by roentgenography. We have noted repeatedly, at the second stage of a 2 stage resection of the right colon, that redundancy had developed

distal to the anastomosis in the end of the proximal segment of bowel after division of the bowel and side-to-side ileocolostomy (Fig. 1b). Such a finding formerly gave us concern, and we have occasionally excised such small redundant segments at the same time that the second stage of the operation was done. However, these short redundant segments had produced no symptoms, they have been observed at necropsy in patients who had lived for prolonged periods without symptoms after operation and, in studies in animals, short loops do not become the sites of complications. We now believe that some redundancy may develop in the end of the proximal segment virtually irrespective of how little bowel has been left beyond the anastomosis and that such redundancy causes no symptoms and gives rise to no complications. It is evident that the mere presence of some redundancy is not an indication for its removal.

The method used to re-establish continuity of the bowel after resection of the terminal portion of the ileum and the right part of the colon varies with the surgeon; end-to-side, end-to-end, and side-to-side anastomosis are all commonly used and each has its advocates. Results following the three methods are comparable, and the risk associated with each seems much the same, at least in the hands of surgeons thoroughly familiar with the particular method used. Since other satisfactory methods are available, it follows that side-to-side anastomosis should probably not be used if the method is to be associated with serious potential hazards. The scarcity of reported cases of serious complications, the rarity of serious complications among our cases and the gross error of technique which must be made to produce the complications in dogs would all argue strongly that complications associated with the blind end of the proximal loop following side-to-side anastomosis are not of great importance and cannot be used to condemn the method. While we are not committed to the exclusive use of any one of the three methods to restore continuity of the bowel after resection, we tend to employ side-to-side anastomosis, particularly after right hemicolectomy (Fig. 1a). With this type of anastomosis the mesenteric attachment to the bowel wall presents no problems and the stoma can always be made of ample size. In short, this method of anastomosis seems easier technically to us than either the end-to-side or the end-to-end methods. It was chiefly because of this preference that the effort was made to evaluate the hazards associated with the inverted end of the proximal segment of bowel. It is evident that complications associated with the inverted proximal end are successfully avoided in the great majority of cases.

CONCLUSIONS

1. The potential hazards associated with the inverted end of the proximal segment of bowel following division of the bowel and side-to-side anastomosis are dilatation and hypertrophy, ulceration, and perforation.

2. Some dilatation and hypertrophy of the proximal end of the bowel distal to the anastomosis develop in many cases but symptoms are rarely produced.

3. When longer than usual lengths of the proximal segment are left distal to the anastomosis symptoms suggestive of partial obstruction may develop. The colicky pains occur in attacks and may be accompanied by vomiting and diarrhea.

4. Complications associated with the inverted end of the proximal loop are unusual as judged by the rarity of the reported cases and by the rarity of cases in our own series. They are largely preventable by avoiding redundant segments of the proximal end of the bowel distal to the anastomosis.

5. Such complications are so unusual that they do not detract from the usefulness of side-to-side anastomosis.

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CALCIFICATION OF THE SUPRASPINATUS TENDON: INFILTRATION THERAPY WITH LOCAL ANESTHESIA AND MULTIPLE NEEDLING

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THE object of this paper is to discuss in detail the infiltration therapy of calcification of the supraspinatus tendon with local anesthesia. The supraspinatus tendon, which is really only one component of the musculotendinous cuff and which is inserted into the greater tuberosity of the humerus, is the victim of degeneration, calcification, and rupture. These three conditions are quite separate clinical entities, but probably result from the same basic anatomical peculiarity of this tendon. The etiology, incidence, pathogenesis, and treatment are described.

GROSS ANATOMY

The supraspinatus tendon, which is one component of a fused structure aptly called by Codman the musculotendinous cuff, is inserted into the greater tuberosity of the humerus. In this region of the shoulder there are many important and interesting anatomical features. The subacromial or subdeltoid bursa, which is really a synovial bursa lies beneath the deltoid muscle, the coracoacromial ligament and the acromion process itself, intervening between these structures and the supraspinatus tendon. The supraspinatus tendon forms part of the floor of this bursa. This bursa is roughly circular and appears to increase in size with age. Its main function is to permit the upper end of the humerus with its capsule to glide easily under the coracoacromial ligament and the acromion process during the movement of abduction. The subacromial bursa is considered to be indispensable in abduction and rotation of the humerus, but it has been removed on more than one occasion, without interfering with the function of the arm. The three short rotators, supraspinatus, infraspinatus, and teres minor tendons flatten out as they approach their insertion and blend almost indistinguishably with the floor of the subacromial bursa and capsule of the shoulder joint. The edges of these tendons are so closely approximated here, that it is often difficult to tell where one stops and the next begins. It is this fused structure that is referred to as the musculotendinous cuff. The average length of the supraspinatus tendon is 2¼ centimeters.

The attachment of the tendons of these short rotator muscles takes place through most of the upper half of the sulcus which is called the anatomic neck of the humerus. The heavier portions of the tendons are inserted on facets situated on the great tuberosity.

The majority of the pathological lesions around this vulnerable area of the shoulder region result from either acute or chronic trauma, and involve not only the musculotendinous cuff, but also the subacromial or subdeltoid bursa. The one may be secondary to the other, so that when considering pathology here all possible lesions must be visualized.

The supraspinatus tendon is subject to degeneration, rupture and calcification, and the subacromial bursa above it to acute or chronic bursitis. The pathology of an acute rupture of the supraspinatus tendon was first recognized by Smith in 1835 and fully described as a clinical entity by Codman in 1911. Acute rupture, partial or complete, due to a sudden abduction violence must be distinguished from a rupture of a few fibers of the tendon, already degenerated by the gradual attrition of the movement of abduction against the prominent acromion process and its associated coracoacromial ligamentous arch. The actual causation of such degeneration is not fully understood. Senile degeneration of the tendon is postulated as one theory, but it occurs in very young adults. It is also suggested that deterioration of blood supply to the tendon may play some important part. Most surgeons, however, are of the opinion that degeneration

is due to the wear, caused by long continued use of the arm in abduction and associated with friction against the coracoacromial arch. Heredity has not yet prepared the human shoulder against the tension and friction of the supraspinatus tendon of the typist, machine worker, or hairdresser. Whether occupation alone causes an ischemia, due to compression of vascular supply or attrition, because of friction is still problematic.

CALCIFICATION OF THE SUPRASPINATUS TENDON

Painter in 1905 was the first to recognize calcium deposits in x-ray films of the shoulder. He believed the shadows he observed were due to a thickening of the subdeltoid bursa. Codman, however, who was present at one of Painter's operations, was the first to realize that the deposit was actually in the supraspinatus tendon. It has been observed that gross pathological anatomy reveals a deposition of calcium in the short tendons of the shoulder capsule, most frequently situated in the supraspinatus tendon. On the base of the subacromial bursa in the tendon involved there is an elevation with a grayish white center and a red turgid periphery (2) resembling a boil (5). It is important to note that the bursa itself contains a fibrinous exudate. The calcium deposit at this stage is soft and creamy and resembles staphylococcal pus, or it may be firmer and of the consistency of tooth paste. The acute symptoms are probably caused by involvement of the base of the subacromial bursa. The calcium deposit may rupture into this bursa, producing a chemical bursitis (according to Bishop) and the site of rupture may often be demonstrated at operation (Brickner).

Microscopically the calcium deposits may occur as a number of foci of varying size embedded in a tendon which shows fibrosis and is infiltrated with masses of chronic inflammatory cells, mostly lymphocytes and plasma cells with a few giant cells. The connective tissue may show hyalinization, according to a description by Moschowitz.

Chemically the composition of the calcium has been reported by many authors (6, 14, 17) as occurring in the form of calcium carbonate and calcium phosphate, and some analyses show calcium oxalate. The analyses have differed greatly as to the proportion in which these calcium salts occur.

INCIDENCE

The only reliable figures of the incidence of calcification of the supraspinatus are those of Bosworth — among 6,c61 supposedly normal persons of the "white collar" class, calcium was found on routine fluoroscopic examination in 165 — 2.7 per cent, in one or both shoulders. In this series the lesions was found most frequently in the period of greatest activity of adult life, nearly all of his subjects being under 50 years of age. It occurs more often in males—3.6 per cent in 1,178—while among 3,883 females it was only 2.5 per cent.

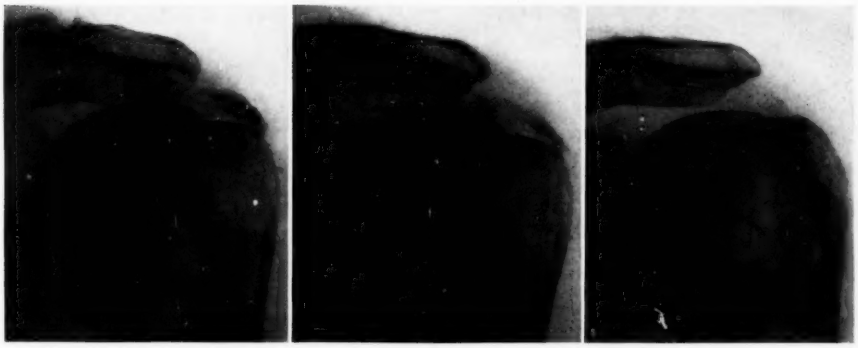
Not every calcification is therefore a subject of symptoms. The soil, however, is fertile for rupture of tendinous fibers with subsequent acute or chronic symptoms.

ETIOLOGY AND PATHOGENESIS

Occupation. Typists, hairdressers, and machinists appear to have a significantly higher incidence of calcium deposits. Long continued use of the arm in abduction seems to be a predisposing feature.

Infection. The assumption that infection plays any part—locally or through septic foci —has never been proved. Many who have operated on these deposits and made bacteriological cultures have found negative results.

The sequence of events leading up to the actual deposition of calcium appear to be primarily an interference of blood supply to the tendon. There is, however, controversy how this is brought about. Codman and Wright advanced the hypothesis that calcium is laid down in the unabsorbed hemorrhage which fills the defect in an abortive attempt at repair of minor traumas to the tendon tissue which normally has a poor blood supply. Moschowitz and Elmslie arrived at a similar conclusion. Carnett recorded his opinion that the deposits are as a rule quiescent in their formation and are due to tendinitis, local necrosis of tendon, and calcification produced by often repeated occupational traumas which squeeze the supraspinatus tendon between the tuberosity of the humerus and the roof of the suba-



a b c

d

Fig. 1. Case 1. Mr. L. W. a, Before infiltration therapy. Note dense calcified mass. b, One day after infiltration therapy, calcification shadow definitely fainter; c, 3 days after initial treatment, almost complete absorption of calcification; d, 4 days after, complete absorption of calcification.

cromial bursa. Wells in discussing the pathology of the calcification concluded as follows: "Any area of dead tissue not infected and so large or so situated to be unabsorbed will probably become infiltrated with lime salts. Next to totally necrotic tissues are masses of scar tissue that have become hyaline subsequent to the shutting off of circulation in the scar by contraction of the tissue above the vessels. The calcium salts come from the blood where they are held in solution or suspension by the proteins of the plasma in an unstable condition capable of being overthrown by the increased alkalinity of the blood resulting from changes in the carbon dioxide content. In the areas to become calcified the circulation is very feeble, the blood plasma seeping through the tissues as through any dead or foreign substance of similar structure without the presence of red corpuscles to permit of oxidative changes and the consequent production of carbon dioxide content. The increased alkalinity resulting from the low carbon dioxide content of the tissue fluids renders the inorganic calcium carbonate and phosphate solution unstable and accounts for the gradual deposition."

Trauma. A single severe trauma does not cause calcification but may precipitate acute symptoms in an already existing deposit. From Bosworth's series of x-ray films of normal shoulders it is firmly established that many people walk around with or without a knowledge of such a calcification in the shoulder. These calcifications are absolutely symptomless until a single trauma or repeated minor traumas, occupational or otherwise, predisposes to acute tendinitis, an acute inflammation with its acute train of symptoms. To a lesser degree such tendinitis may cause the subacute or chronic symptoms of supraspinatus calcification. The pathogenesis of such trauma has already been discussed and it is on the feasibility of the diminished blood supply theory that the rationale of this infiltration therapy is put forward.

Clinical features. The symptoms in general bear no relation to the size or duration of the calcareous deposit, or to the amount of inflammatory reaction at the base of the subacromial bursa. It is generally believed that deposition of lime salts precedes by weeks, months, or years the onset of clinical symptoms. After

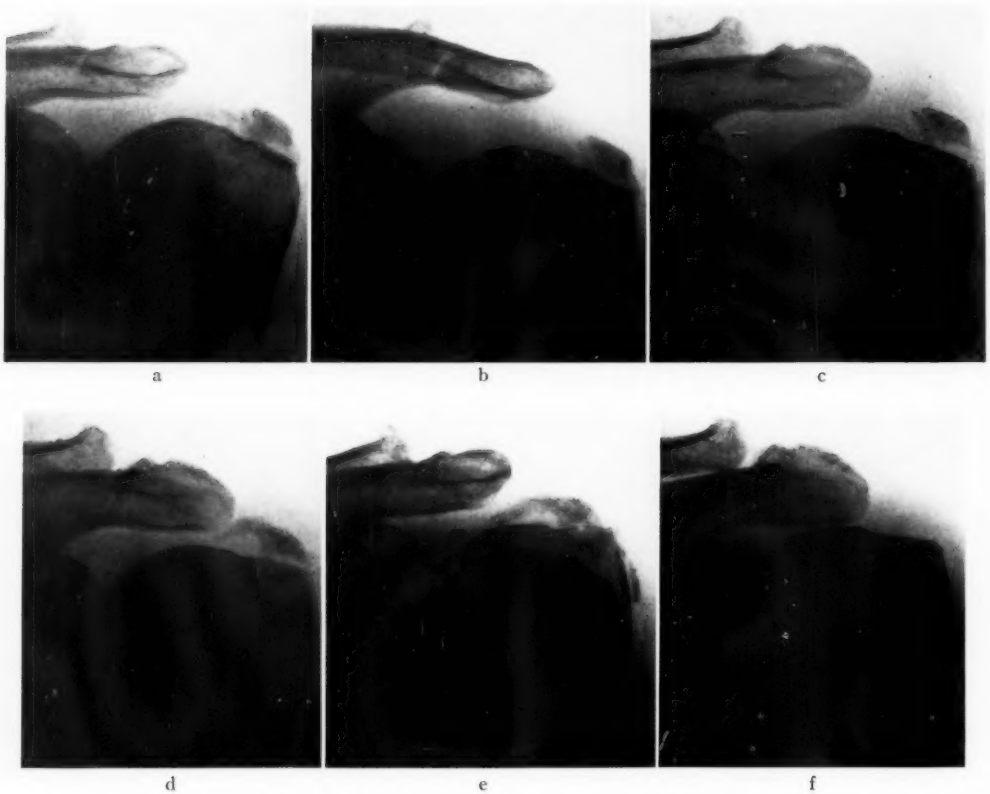


Fig. 2. Case 2. Mrs. J. Y. a, Calcified supraspinatus 1 day before treatment; b, 1 day after infiltration and movement; c, 8 days after. Note absorption of periphery; d, 12 days after infiltration treatment, calcification becoming more "woolly" and elongating; e, 23 days after, calcification "overflowing its banks"; f, 36 days after initial treatment, almost complete absorption after having "overflown its banks."

the deposit has formed mild trauma will produce in some the acute inflammation with characteristic symptoms, or in others chronic signs and symptoms. Acute symptoms may even be superimposed on the chronic condition. Calcium deposits have been observed to disappear with and without treatment. The acute inflammation with its increased blood supply and accumulation of inflammatory cells "steps up" the local metabolite rate with subsequent production of carbon dioxide in sufficient amount to lead gradually to dissolution of the calcareous deposits. An acutely inflamed deposit may rupture into the subacromial bursa, setting up a bursitis. This may also perhaps explain the acute attacks in which there is rapid recovery without treatment.

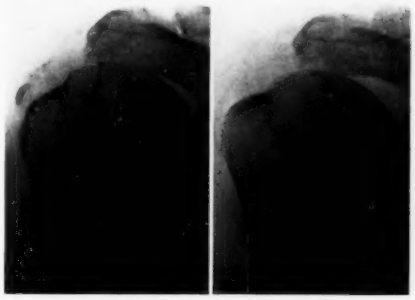
Acute phase. An acute attack may appear without warning, even during sleep, or it may follow some abduction type of trauma such as preventing an object from falling with the arm in extreme abduction; a fall on the outstretched hand, or sudden forcible abduction. It may also develop during the course of a subacute or chronic attack. The patient immediately develops excruciating pain, abrupt and vicious, with complete limitation of all movements at the shoulder joint. The pain is felt over the bursa and over the insertion of the deltoid muscle. The pain produces reflex spasm of the

whole shoulder girdle causing pain down the arm and forearm, even into the fingers, which is so often diagnosed as "acute brachial neuritis." It is possible that such a neuritis is really the acute phase of supraspinatus calcification. This reflex spasm is known to produce the typical clinical picture of the "scalenus anterior syndrome" on the affected side.

Atrophy of the spinatus muscles occurs if the symptoms last more than a few weeks. A lump may be felt just medial to the greater tuberosity if the deposit is in the supraspinatus tendon. If untreated such an acute phase may last for several weeks and then revert to a chronic type with the possibility of adhesion formation, or it may clear up fairly rapidly, especially if the deposit ruptures into the subacromial bursa.

Chronic phase. The onset is insidious. First there is an uncomfortable feeling around the shoulder, later it is hard to find a comfortable position in which to rest the arm at night during elevation of the arm in the coronal plane. Pain is most often felt at the fibers of insertion of the deltoid muscle, while the maximum point of tenderness is over the deposit in the tendon close to the greater tuberosity. If there has been a long painful period the whole area becomes sensitive with pains shooting up into the neck and down to the hand. This has given rise to the misnomer "chronic brachial neuritis." In some cases the hand has been seen to swell and the skin to become atrophic. There is usually a certain amount of spasm and limitation of abduction and external rotation at this point. Definite painful "hitches" associated with abduction through 70 to 100 degrees, are commonly present and referred to as Dawbarn's sign when the painful "hitch" reappears through the same arc on the descent of the arm. Acute exacerbations may occur at any time during the chronic course.

X-ray examinations. For all suspect cases of calcification of the supraspinatus x-ray investigations should be employed and spot roentgenograms taken as suggested by Bishop. The deposit must be seen in profile, or it will be obscured by the underlying bone. Deposits of calcification may be single or multiple and if liquid may be seen to change its shape with movement. Sometimes at operation a milky fluid containing calcium has been found, which did not show up on x-ray examination.



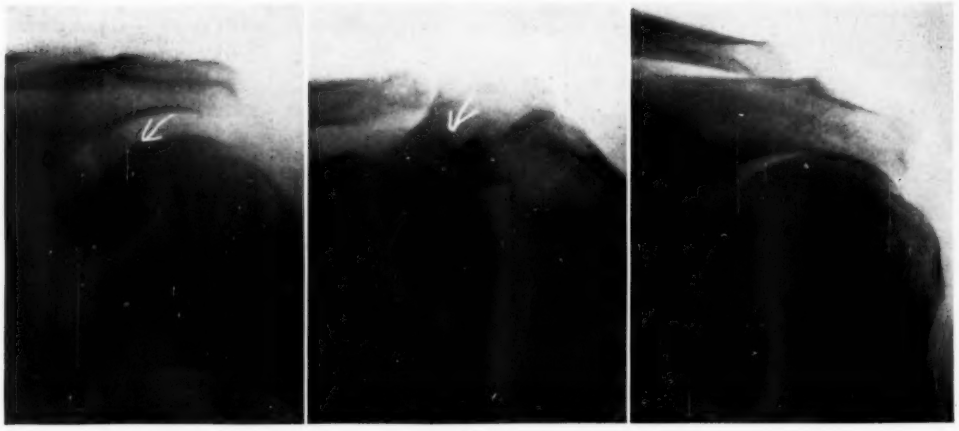
a b

Fig. 3. Case 3. Mr. J. J. H. a, Before infiltration and movements; b, 3 days after almost complete absorption. Note here also dissemination of calcified deposit beyond its original confines.

Diagnosis. The diagnosis of the acute phase is usually confirmed and fairly easily established by a history of "something wrong," previously in the shoulder, aggravated by some slight trauma. The acute symptoms are often excruciating with almost complete limitation of movement of the shoulder. A localized area of maximum tenderness below the tip of the acromion process—a painful "hitch" on abduction and again on descent—and the disappearance of the tenderness of the fully abducted arm, beneath the tip of the acromion are of sufficient importance to diagnose pathology in the supraspinatus tendon in the lesser acute lesion. The x-ray appearances are pathognomonic, especially if these are of the semi-soft technique. Calcification in a milky form containing calcium has been known to be present without showing up on test x-ray films (2).

TREATMENT

Chronic phase. The efficiency of treatment of the chronic forms is difficult to evaluate, because the patient will get better in spite of any real form of active therapy, although it may take up to 2 years for the deposit to become absorbed. Removal of the calcium by operation gives the most satisfactory result, although recovery is slower than in the case of an acute deposit. Patients, however, always prefer some form of heat therapy, and over a period of time they recover. The increased



a b c

Fig. 4. Case 4. Mr. J. A. G. a, b, Before infiltration therapy; c, 11 days after, complete absorption.

vascularity with heat therapy and deep x-ray therapy, and the resulting high carbon dioxide content of the tissue makes the medium acid, so that calcium is absorbed. The use of immobilization in abduction causes adhesions and is mentioned only to be completely condemned. Active repeated movement must be the golden rule from the very onset of therapy.

Acute phase. Many forms of treatment have been advocated for the acute attack. Most authors, Hitzrot, Bosworth, Codman, Moseley, appear to favor excision of the deposit through the same incision as exposure for a ruptured supraspinatus tendon. Irrigation by the two needle method of Patterson and Darrach has been advocated for acute attacks. It is an operative procedure and while good results have been reported by those who favor the method it is not very satisfactory for solid calcium. Short-wave diathermy and deep x-ray therapy are advocated to produce hyperemia to aid rapid absorption of the calcified deposit.

It is proposed in this paper to describe in detail the treatment employed by the author for the past 5 years, for the acute form of supraspinatus calcification. It was felt that in accepting Well's hypothesis for pathological calcification, a more simple method of rendering the medium acid could be achieved, than a surgical operation. The method employed is local anesthetic infiltration of the calcification and multiple needling of the deposit or whatever capsule may envelope it. This is followed by immediate and continuous movement of the affected shoulder.

Technique of infiltration therapy. The acute cases only are handled with this method as experience has shown that the more acute the pain and the more limited the movement the better are the results.

The patient is either seated or lying, and after thorough cleansing of the skin, the area around the acromion process is infiltrated with 1 per cent novocain or procaine solution. The deeper structures are gradually anesthetized and the needle is passed almost horizontally and slightly backward, keeping it just parallel to the under surface of the acromion process all the time. These deeper structures must be well infiltrated otherwise the patient experiences excruciating pain. When the deposit is reached it is easily recognized by a grating sensation. The needle is then changed to a fairly wide bore. The deposit is then thoroughly infiltrated with another 10 to 15 cubic centimeters of 1 per cent novocain, changing the direction of the needle all the time as the fluid is injected. After the infiltration, the needle is repeatedly withdrawn from the deposit and reintroduced about 7 to 10 times (the needle is not withdrawn from the skin in performing these multiple pricks). The usual care is

Fig. 5. Case 5. Mr. C. K. a, left, Extensive calcified mass before infiltration therapy; b, 28 days after, almost complete absorption.

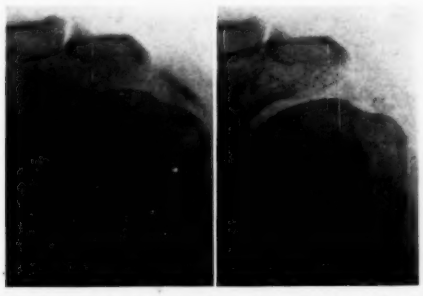


Fig. 6. Case 6. Mrs. E. G. a, left, Before infiltration; b, 23 days after, almost complete absorption.

taken to determine any sensitivity to the local anesthetizing fluid employed. It is essential to carry out these injections carefully, and gradually and to see that the needle is in the deposit each time it is withdrawn and reintroduced. In about 10 to 30 minutes, varying with each case, the acute agonizing pain disappears and the completely immobilized shoulder can now be moved fairly freely in all directions. The patient is instructed in all movements of the shoulder, especially full 180 degree abduction, internal and external rotation. A fully experienced trained physiotherapist is employed to instruct the patient in all these movements. The patients are very happy about the miraculous relief of pain effected by this local anesthetic injection, but they must be informed that such relief is to be short-lived and that the pain will recur and perhaps be even worse in a few hours.

The stiffness, however, does not reappear to the same extent, and the patients are impressed with the necessity of continuing the movements of the shoulder no matter how limited or painful. These injections are preferably carried out in the morning so that movements can be continued in the afternoon. Sedatives are prescribed for the recurrence of the pain.

The patient is seen thereafter daily to ascertain and instruct movement of the shoulder, and if necessary daily x-ray films are carried out to note the progress of absorption of the calcified deposit. The pain although worse soon after the injection is better the next day and gradually improves and in the majority of our cases the acute pain disappeared in an average of 10 days. The relief from pain is proportionate to the rate of absorption of the calcification. If the movements are diligently and intelligently carried out, then the rate of absorption of the calcification is complete in an average of 3 to 4 weeks. Radiant heat to the shoulder was utilized in those patients who experienced more pain than anticipated.

RATIONALE OF INFILTRATION THERAPY

The rationale of this infiltration therapy depends on the production of hyperemia in the region of the shoulder. This is achieved by allowing the shoulder to move in all directions as soon as possible, and which is made possible only by the use of a local anesthetic. The local anesthetic therefore is not the active principle of this therapy, but merely an aid to the production of hyperemia. Secondly, the repeated

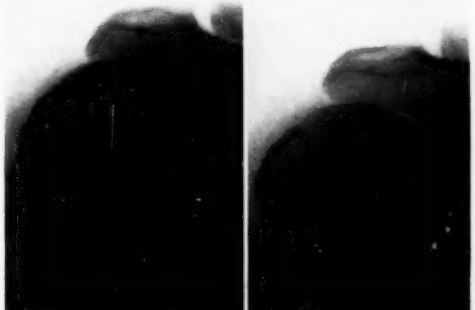


Fig. 7. Case 7. Mr. H. McM. a, left, Before infiltration, faint shadow but markedly acute symptoms; b, 14 days after, complete absorption.

TABLE I.—SUMMARY OF 7 CASES

Case occupation	Previous history X-ray appearance	Treatment	Relief and rate of absorption of deposit	Follow-up
1. Mr. L. W. Storeman	Chronic pain for months. No trauma. Sudden acute agonizing pain. Extensive calcified deposit of supraspinatus.	1 infiltration 10 c.c. procaine 1% with 10 c.c. normal saline. Movements. Multiple needling.	Immediate relief, pain returned in 3 hours, but movements remained improved. Deposit absorbed in 5 days. See Figs. 1a – 1d.	2 years after no pain and full movement. No recurrence.
2. Mrs. J. Y. Housewife	Gradual pain for 6 days—then sudden acute onset. No trauma. Extensive calcification of supraspinatus.	1 infiltration 15 c.c. procaine 1% with movements. Multiple needling.	Immediate relief. Pain returned worse in 1 hour. Deposit ruptured into surrounding area—overflowing its banks. Almost complete absorption 36 days. See Figs. 2a – 2f.	18 months after no reccurrence of pain or limitation of movement.
3. Mr. J. J. H. Boot repairer	No previous history, but wrenched shoulder on tram (streetcar) in abducted position. Fragmented calcification of supraspinatus.	1 infiltration 15 c.c. procaine 1% with 7 c.c. normal saline. Movements. Multiple needling.	Immediate relief for about 3 hours—more movement. Almost complete absorption in 4 days. Faint rim left. See Figs. 3a and 3b.	Lived out of town. Could not return for x-ray, but regular communications for 4 years after had full movement—no pain.
4. Mr. J. A. G Active farmer	No previous history. No trauma. Sudden acute agonizing pain and stiff shoulder. Rounded and fragmented calcification.	1 infiltration 20 c.c. procaine 1%. Movements. Multiple needling.	Immediate relief lasting 2 hours. Good movements thereafter. 11 days complete absorption. See Figs. 4a – 4c.	X-rays 7 months after showed no recurrence. Communication up to 4 years after—full movement—no pain.
5. Mr. C. K. Hairdresser	Previous gradual ache. Then sudden acute pain and stiff shoulder. Very extensive and fragmented calcification.	1 infiltration 15 c.c. procaine 2%. Movements. Multiple needling.	Immediate relief for 6 hours: recurred as bad, but movements better. Almost complete absorption in 28 days. See Figs. 5a and 5b.	2 years later no recurrence of calcification, pain, or stiffness.
6. Mrs. E. L. Housekeeper, cook	First noticed pain in shoulder 3 months previously; diagnosed as rheumatism. Suddenly without trauma acute phase. Elongated, linear calcification.	1 infiltration 15 c.c. procaine 1%. Movements. Multiple needling.	Immediate relief lasting for 3 hours. Complete absorption 30 days after. See Figs. 6a and 6b.	9 months follow-up showed no recurrence of calcification, pain or limitation of movement.
7. Mr. H. McM. Accountant	No previous history. Sudden wrench at squash. Acute agonizing pain with limited movement. Very faint fragmented calcification.	1 infiltration 15 c.c. 2%. Movements. Multiple needling.	Immediate relief and movements lasting 5 hours. Recurred worse than before, but movements better. Complete absorption in 8 days. See Figs. 7a and 7b.	4 years after, no recurrence of calcification, pain, or limitation of movement.

multiple puncturing of the deposit, allows the soft calcification to "overflow its banks," (Case 2, Fig. 2e), thereby disseminating the calcification into surrounding planes, which in turn absorbs it at a quicker rate. It has been observed by Wilson that an inflamed calcified deposit may rupture into the subacromial bursa, setting up a bursitis; this may perhaps explain the acute attacks with rapid recovery without treatment as described by Codman.

The mechanical irritation produced by the needle usually results in infiltration of inflammatory cells which increases local metabolism which in turn helps absorb the calcification.

The sum total of all these factors hastens the absorption of the calcified deposit and in actual practice this form of therapy has been highly successful in 15 cases. Many of the failures of this method are probably due, first, to inadequate infiltration and needling of the deposit, and second, to lack of immediate and daily movement of the shoulder joint. The recurrence of the pain, which as already stated is very often worse than the original discomfort, has led orthopedic surgeons and others to condemn this form of treatment, but perseverance and the use of sedatives can easily overcome this discomfort. Many are apt to expect too much at once with a single needling of the deposit. If this technique is carried out many excisions of calcified supraspinatus deposits can be avoided, which is after all an operation like any other. This infiltration and needling therapy is simple, quick, and can be carried out with the patient ambulatory. Not more than one injection has been necessary in the real acute case, although two and more have been used for the subacute phase.

This infiltration therapy has been used in a few cases of acute painful shoulder with localized subacromial tenderness and especially in those associated with a painful "hitch," but without a calcareous deposit. In these the results have been most favorable and the relief as dramatic and prompt as the tendinitis with calcification. It is possible that in these shoulders the musculotendinous cuff is in the precalcification phase. This therapy has not been used for the calcification found accidentally.

The amount of local anesthetic fluid injected appears to have no direct influence upon the results obtained, except that the solutions should be injected directly into the deposit. If there is any doubt as to the exact location of the needle x-rays of the needle *in situ* are taken to determine the exact position.

No originality is claimed for this form of infiltration therapy. As far back as 1913 Flint of Yale reported prompt relief of symptoms by aspiration under local anesthesia. A year later Sievers (1914) in Germany, cognizant of Flint's publication described the case of another patient similarly treated with success — Haldeman and Hall, Haggart and Allen, and Ferguson have all described the use of local anesthesia for painful shoulders, but many appear to have confused acute subacromial bursitis and true calcification. Lapidus in an excellent article on acute tendinitis with calcification describes this infiltration therapy with marked success in 16 cases of the acute phase of calcified tendinitis of the shoulder. He also includes collectively similar conditions around the elbow, hip, knee, and wrist joints and refers to them there as acute tendinitis with calcification which are treated with similar favorable results by this infiltration therapy.

Results. Fifteen patients have been treated with this method with a follow-up of periods varying from 7 months to 4 years. Table I summarizes 7 of these cases. The accompanying x-ray films show the rapid, complete absorption with this local anesthesia infiltration, multiple needling, and movement therapy.

SUMMARY

The gross anatomy of the musculotendinous cuff of which the supraspinatus tendon is a component, is described. The pathogenesis and etiological factors of calcification are subject to wide difference of opinion, but occupation appears to play an important rôle. The actual deposit of calcium is believed to be due to a low carbon dioxide content and a consequent high alkalinity resulting from a diminished blood supply. The incidence of calcification in individuals with no symptoms is 2.7 per cent in the largest reliable series of 12,122 persons, detected on routine x-ray examinations.

The close relationship of trauma to the deposition of calcium salts in the supraspinatus tendon may be explained by the rupture of some of the degenerated fibers producing an acute or chronic tendinitis. This phase probably causes the acute or chronic symptoms.

The acute and chronic phases are described, and also the various treatments recommended.

A simple nonoperative therapy of local anesthesia infiltration and multiple injections of the deposit is described together with a detailed description of 7 cases. An essential feature of this therapy is immediate and continued movement of the shoulder joint.

Reproduction of x-ray films are presented illustrating the rapid absorption of the calcified deposits in the acute lesions only, and one series especially depicting the calcareous deposit "overflowing its banks" into the surrounding tissues.

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THE INDICATION FOR POSTERIOR TRANSPLEURAL BRONCHOTOMY IN THE MANAGEMENT OF INTRABRONCHIAL TUMORS

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BY posterior transpleural bronchotomy is meant an opening made in the posterior or membranous portion of the bronchus, after this structure has been exposed by transpleural thoracotomy.

Conclusions based on experience with a single case are obviously to be regarded as provisional because such experience is inadequate to justify approval or condemnation of any surgical procedure. However, because of the rarity of the clinical picture which lead us to use this approach and the very gratifying end-result obtained in this case, we feel compelled to add such experience to the literature.

Eloesser in 1940 reported the use of this procedure and Goldman referred to the exhibition of bronchotomy in the management of bronchial tumors in May, 1946, but the recent literature fails to indicate any use of this approach otherwise.

Assuming that the recent advances in the control of infection, as well as thoracic surgery in general, now permit this approach to be practical, its position in such evolution would properly fall one step ahead of segmental resection in aiming at eradication of disease with minimal sacrifice of useful lung. Thus, after thoracic surgery had passed from its incipient phases and intrathoracic procedures became relatively standardized, resection in the form of lobectomy or pneumonectomy was the preferred treatment for many types of pathologic states. As the details of anatomy of the segmental hila became well understood, conservation of undamaged lung tissue by resection of the involved segments only, emerged as the ideal. Now as a further step along these lines, judgment is required of this ultimate attitude in the conservation of lung.

Bronchotomy is not a new term nor is it a recently conceived operative procedure, but must be considered as a revival of an old concept which perhaps only now is of practical application due to the present day adjuncts to surgery, namely, anesthesia and antibiotic therapy.

Bronchial obstruction has interested physicians for a long time. Without entering into a complete review of the literature, the developmental history of the management of this condition can be outlined.

Inhaled foreign bodies were the chief concern of the older physicians. The interest in other forms of bronchial obstruction such as tumors, had to await the introduction of bronchoscopy by Killian (1897) and its expansion by C. Jackson (1904).

DeForrest Willard in 1891, conducted animal experiments to explore the feasibility of removing intrabronchial foreign bodies by a transthoracic bronchotomy. Prior to this time, inhaled foreign bodies were treated by tracheotomy, often called bronchotomy, followed by blind grappling within the air passages for the offending agent. Such procedures were not very successful and the principle dependence was on spontaneous expulsion, the tracheotomy wound serving as an easier avenue of escape than the rima glottis. In those days, the difficulties that were presented to a surgeon dissecting into the hilum of the lung were considered quite unsurmountable. Nevertheless, bronchotomy either by a transpleural or transmediastinal approach was attempted in the succeeding years. Most of them ended fatally either eventually or immediately (1, 2),

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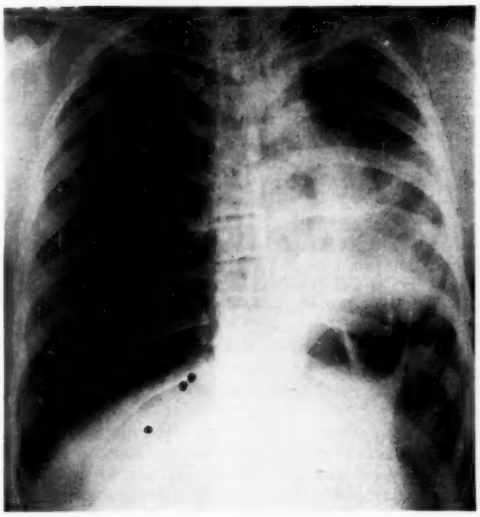

Fig. 1. Roentgenogram of November 20, 1946, showing the atelectasis of the lower lobe.

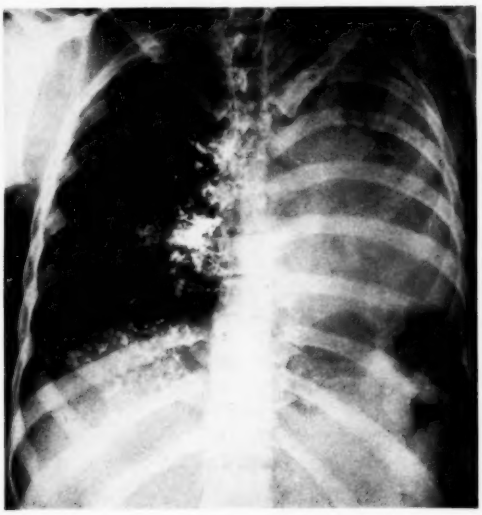

Fig. 2. Roentgenogram of December 10, 1946, showing evidence of progressive obstruction now involving the upper lobe as well as the lower. The lipiodol is residual from an earlier bronchogram.

but a successful one was performed, for example, by Goeltz in August, 1904.

With the perfection of bronchoscopy, attention seems to have become focused on this accurate and logical means of attacking problems of intrabronchial pathology. As the sequelae of bronchial obstruction become understood and emphasized, resection of the involved lobe or segment thereof become the treatment of choice, not only for foreign bodies inaccessible to endoscopic management, but also for tumors not manageable by this approach (8).

If speculation is permissible, the idealized indication for bronchotomy in the relief of neoplastic bronchial obstruction would involve a benign, pedunculated tumor, not manageable endoscopically, obstructing a stem bronchus without irreversible lung damage distal to it. A stem bronchus is chosen because in the present state of our experience, such a tumor involving a lobar bronchus only, would be handled by lobectomy with a very high degree of safety.

The hazards anticipated in performing bronchotomy must include at least (1) the grave danger of pleural and mediastinal contamination by the secretions retained distal to the obstruction; (2) the reticence with which the affected lung or lobe will re-expand following relief of the obstruction, enhancing, therefore, the danger of empyema; (3) the leaving of the patient with a severely diseased lobe or lung, most probably in the form of bronchiectasis; (4) the possibility of tension pneumothorax, or mediastinal emphysema

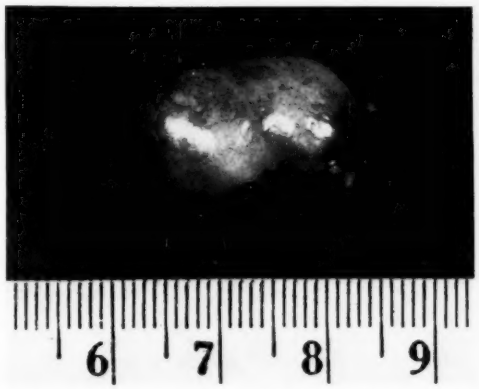

Fig. 3. Photograph of excised endobronchial tumor, against a centimeter scale. The very narrow pedicle is clearly shown.

Fig. 4. Early postoperative roentgenogram showing evidence of reaeration of the left lung. The left pleural cavity contains a loculated effusion not being adequately evacuated by the drains. Although it was feared that organization might occur, a satisfactory resorption took place.

from a leak at the site of bronchial incision; and (5) the possibility of a bronchial stenosis developing at the site of bronchial suture.

CASE REPORT

J. E. F., male, white, age 26 years. The history of chest disease began in March, 1946, while patient was working as a welder, at which time he noted the rather sudden onset of a cough accompanied by shortness of breath. He consulted a physician, who advised hospitalization. Instead of accepting this advice he returned to work after a week. The cough and shortnesss of breath had abated somewhat but were still present and seemed to become progressively more noticeable. In November of 1946, he was definitely worse and dyspnea was severe. A roentgenogram taken at that time revealed atelectasis of the left lower lobe (Fig. 1). Bronchoscopy was reported as revealing an intrabronchial mass completely obstructing the left lower lobe.

By the time of admission to our care, his condition had deteriorated noticeably. Dyspnea was so severe that oxygen was required even when he was recumbent. Fever to 104 degrees of a septic type was present. The roentgenogram (Fig. 2) indicated now that the upper lobe was also obstructed, the sepsis being no doubt due to the extensive retention of sputum in this completely atelectatic left lung.

As soon after admission as seemed permissible, a bronchoscopic examination was carried out (December 21, 1946). This examination revealed a normal appearing trachea and right bronchial tree. Some 2 centimeters from the coryna on the left, however, the lumen was completely obstructed by a rounded mass which was smooth, not ulcerated, rather glistening in appearance and pink in color. The mass was firm in consistency but resilient in character. It could not be displaced downward in the bronchial tree, even though at no point of its circumference, as this disappeared from view in the bronchial lumen, could any attachment to the bronchial wall be discerned. The long aspirating cannula could be slipped past this mass without significant difficulty and pus could be aspirated from beyond it. The impression was distinctly created that this mass had extended up the bronchial lumen but was probably pedunculated. By no maneuver could the pedicle be visualized and the obvious longitudinal extent of the mass precluded prompt removal by endoscopic route. A biopsy was taken.

This procedure brought about some improvement in his clinical condition, even though no evidence of aeration in this lung was afforded. The biopsy was reported as indicating a benign tumor, ultimately classified as a fibroma, (Fig. 7).

On December 24, 1946, the thorax was opened, having in mind carrying out a left lower lobe lobectomy and extracting the tumor from the upper reaches of the bronchial tree. It was found, however, that both lobes were completely consolidated and that a pneumonectomy would have to be done as the safest form of resection. Since the tumor was benign by biopsy and in all probability pedunculated,

Fig. 5. Roentgenogram taken approximately 1 month after operation, showing a very gratifying return to normal.

it was decided to explore its resectability by open bronchotomy. The lung was rotated forward and the bronchus dissected free. An incision was made into the posterior membranous portion longitudinally where the tumor was palpable. The tumor promptly herniated through this incision as if under pressure. The incision was carried distally following the course of the tumor, down to a very narrow stalk from which it arose in the roof of the dorsal branch bronchus to the lower lobe. An area of mucosa was excised at the point of attachment of this stalk (Fig. 3). Much purulent sputum was aspirated from the bronchial tree and all branches were cleaned as completely as possible by catheter suction. The bronchial incision was closed with interrupted silk sutures in one layer and the thorax was closed in routine manner, with drainage by an anterior and posterior intercostal catheter.

The postoperative course was gratifyingly benign, the lung progressively aerating and expanding to fill the hemithorax. The fever subsided as the retained secretions were coughed up. Five weeks following the operation, the chest was virtually normal by roentgenogram, there was surprisingly little evidence of bronchiectasis by bronchography, the bronchial lumen was normal on bronchoscopic examination except for a very small ridge at the site of suture, and symptoms were rapidly disappearing. The only postoperative complication was the presence of a mild jaundice of undetermined etiology (Figs. 4, 5, and 6).

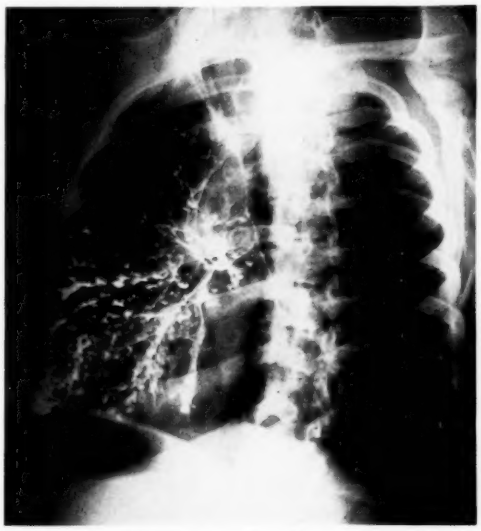

Fig. 6. Bronchogram approximately 1 month postoperative. Although changes are seen in this bronchial tree, they are not very advanced. Cough was rapidly abating and sputum was being raised only in small and decreasing amounts.

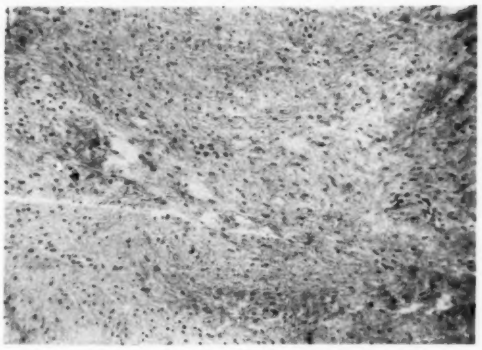

Fig. 7. Histologic appearance of the tumor. After differential staining, this tumor was considered as being in the fibrocytic class rather than of smooth muscle origin. Diagnosis: fibroma. (Courtesy of Dr. W. L. McNamara, Veterans Administration Hospital, Hines, Illinois).

When compared to the case reported by Eloesser, certain differences are noted. In his case, the history was one of intermittent bronchial obstruction over a period of 4 to 5 years; there had occurred a suppurative complication requiring surgical drainage, from which a bronchocutaneous fistula had apparently persisted; the tumor was not visualized even by repeated bronchoscopic examinations; the neoplasm was ultimately classed as a carcinoma; and, finally, from the standpoint of technique, the bronchus was incised transversely and this incision later extended.

In our case, the clinical and roentgenologic data indicated a progressive type of bronchial obstruction of relatively short duration (9 to 10 months) and there had been no suppurative complication requiring surgical drainage; the benign character of the tumor and the level of the obstruction was well understood preoperatively; and finally, the bronchus was incised longitudinally.

Certain points in technique may be worth recording.

1. The position of the patient on the table seems to be of importance, and the use of the "face down" position as described by Overholt so disposes the hilum that the long axis of the bronchus is accessible in a roughly horizontal manner for ease of surgical manipulation. It further tends to favor the displacement of the lung in such a way that the main

lobar branches of the bronchial tree are relatively dependent from the main stem bronchus, thereby making control of the retained secretions easier.

2. The bronchus is cleared over a sufficient length of its course to insure adequate room. It was steadied in our case by a proximal and distal loop of umbilical tape. The use of staysutures as mentioned by Eloesser seems to carry the possibility of incorporating the tumor as well as the bronchial wall in one or both of them. In our dissection of the bronchus, no particular attention was paid to the boundaries of the mediastinum, our intention being rather to clear an adequate length of the bronchus as determined by palpation of the tumor.

3. The mediastinum was not closed by suture but was thus allowed free drainage into the pleura.

4. A longitudinal incision in the bronchus seems to offer the best possible exposure and affords an incision that is easily reparable.

5. Ample drainage of the pleura should be provided because these lungs are all probably slow in expanding and the hazard of empyema would seem to be thereby lessened.

In our case the lung re-expanded steadily but slowly and the fear that the pleural fluid may have become organized was experienced (Fig. 4). However, this possible complication did not materialize.

Antibiotics and chemotherapy both systemically and intrapleurally were used intensively. The drains were removed only after they had ceased to function.

SUMMARY

1. A case is reported in which a benign pedunculated intrabronchial tumor (fibroma) was managed by posterior transpleural bronchotomy with excellent results.

2. A general discussion of the posterior transpleural surgical approach is presented and a few technical considerations arising from the experience in this case are pointed out.

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LARYNGECTOMY

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IN the treatment of carcinoma of the larynx the only hope of survival for the patient lies in complete eradication of the growth. In determining the method of treatment one must bear in mind that untreated cancer is a fatal disease, that the saving of life is the primary consideration of therapy, and that voice impairment or loss of the larynx is of secondary importance.

That eradication of carcinoma can be accomplished in selected cases by laryngofissure has been amply demonstrated by reports in medical literature and a personal experience of 273 cases, of which 188 patients were treated 5 or more years ago. It also has been shown that in certain cases satisfactory results can be secured by irradiation. Viewing the subject purely in the abstract, however, there can be no question that laryngectomy offers a greater degree of security from a life expectancy standpoint than laryngofissure or irradiation therapy but there is much greater disability.

Surgeons are agreed that, as a rule, one chance is given to cure a patient with carcinoma; this applies definitely to carcinoma of the larynx. Patients and many physicians are of the opinion that there can be a choice between irradiation and conservative or radical surgical treatment with end-results about equal irrespective of the laryngeal lesion. There must be definite indications for these therapeutic measures if patients with carcinoma of the larynx are to survive. If one inclines too much to the side of conservatism, is influenced by the patient or his family to save the larynx, or lacks the courage to do a more radical operation, the patient often will pay with his life. I cannot agree with those who believe that laryngectomy still can be performed and good results obtained if there is recurrence of the carcinoma following laryngofissure or irradiation therapy. My statistics indicate that in these, metastasis to regional lymph nodes is of common occurrence, and that laryngectomy, performed as a secondary procedure frequently proves inadequate. It again emphasizes that whoever treats the patient first has the best chance to get him well.

In my experience the most common cause of failure was an inaccurate estimate of the true extent of the carcinoma. It often is difficult to determine the extent even of early carcinoma. In a study of 188 cases of presumably early carcinomas treated by laryngofissure 5 or more years ago, metastasis to regional lymph nodes or distant structures occurred in 12 cases and local recurrence in the larynx in 27. In checking the location of the primary carcinoma in the 27 cases of local recurrence, all were found to have involved either the anterior commissure or the subglottic area. It is evident that laryngectomy should have been the primary surgical procedure in these cases. It is of interest to note that local recurrence after laryngofissure was observed more than twice as often as metastasis to regional lymph nodes or distant organs; local recurrence is uncommon if an orthodox laryngectomy has been performed.

INDICATIONS

The indications for laryngectomy have often been discussed and should be well understood. In selecting the method of treatment the criteria to be considered are the extent and location of the growth, disturbances in motility of a vocal cord or arytenoid, the grade of malignancy, the presence or absence of metastasis, and finally the condition of the patient. Determination of the primary location and extent of the growth should be relatively easy since practically all laryngeal carcinomas are of the squamous cell variety and therefore are surface growths. In addition a majority primarily involve the anterior one-half of a vocal cord, commonly extend forward and downward, and should be readily visualized by either mirror or direct laryngoscopy. In spite of this, however, it has been the experience of all laryngologists that the extent of the

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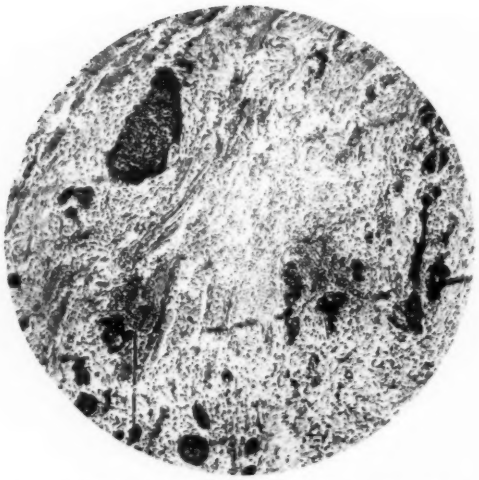

Fig. 1. Photomicrograph from a laryngofissure specimen, in a case of cordal carcinoma that clinically appeared as an early superficial lesion. Clumps of epithelial cells were found infiltrating the cricothyroid muscle, a part of which had been removed at the time of operation. × 33.

Fig. 2. The larynx having been skeletonized, with traction on the hyoid bone the margin of the epiglottis can be visualized. Before the pharynx is opened a No. 0 chromic suture on a nontraumatic needle then is passed through the mucosa and fascia between the epiglottis and base of the tongue as shown in the illustration. When this suture is tied the tissue is "gathered." A transverse incision then is made through the mucosa along the edge of the epiglottis (shown by dotted line) and separation continued along its margins. The upper and lateral limits of the lesion can then be visualized.

lesion usually is greater than appears on the surface. I often have been impressed with Mackenty's statement that "it is wise to add two-thirds to the visible portion of the growth in estimating its actual size."

In addition to determining the extent of the surface involvement it is important to recall that submucosal extension continues beyond surface margins. New and Fletcher studied a group of cases of carcinoma and found that, with the exception of grade 1 carcinoma, there was extension of the growth varying from a few millimeters to as much as 15 millimeters from its apparent margins. The average extension of all grades of carcinoma was 5.5 millimeters.

My experience with lesions in the anterior commissure has shown that in spite of treatment by a radical form of laryngofissure consisting of removal of a triangular segment of the thyroid cartilage together with portions of both vocal cords and an apparently adequate margin of surrounding normal tissue results have been unfavorable (3). Recurrences have been more common in this group than in any other, in spite of the scant lymphatic drainage in the anterior larynx. It is possible that Broyles, who directed attention to the tendinous attachment of the anterior end of the vocal cord to the thyroid cartilage and the absence of a perichondrium, has provided the explanation. Carcinoma in the anterior commissure may extend along this tendon to the cartilage without necessarily manifesting itself as a surface lesion in the anterior end of the cord. Involvement of cartilage is rarely suspected before operation and early involvement may manifest itself only by slight roughening of the cartilage. This normally exists at the attachment of the cords anteriorly. There also may be extension of the growth outside of the larynx corresponding to the cricothyroid membrane without demonstrable metastasis to the pretracheal lymph nodes. In

Fig. 3. With the tied chromic suture held taut and traction made on the hyoid bone, the cut edges of the pharyngeal mucosa can be approximated by continuous suture as it is separated from the larynx.

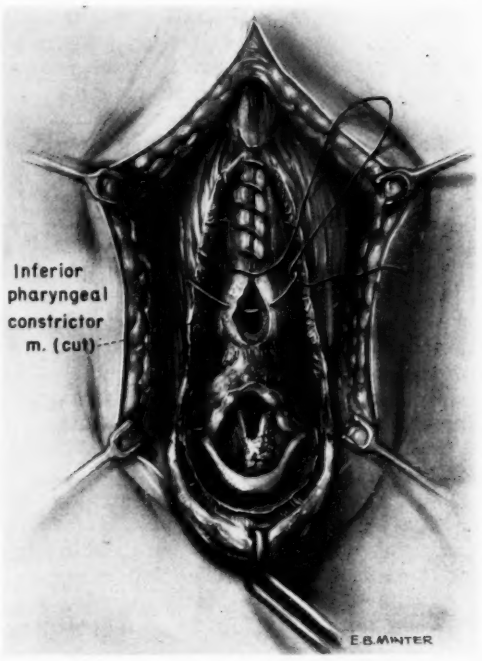

Fig. 4. This illustration shows closing of the pharyngeal stoma by continuous chromic suture. (This suture should be held taut by an assistant). It is important that the raw surfaces and not the mucosa are approximated. With completion of this suture the cut edges of the inferior constrictor of the pharynx and its fascia are approximated and an additional third layer of interrupted sutures is placed to help obliterate the space. Complete skeletonizing down to the tracheal mucosa should be done before the airway is opened.

addition, the carcinoma may extend to the cricothyroid muscle, yet appear as an early cordal lesion (Fig. 1). New and Fletcher found that in 32 specimens in which carcinoma could be demonstrated inside the cartilage there were 11 in which the growth was also present outside the cartilage. I am convinced that if anterior commissure lesions are treated by laryngectomy there will be fewer recurrences in these cases. In the 27 cases of local recurrence of carcinoma in the larynx following laryngofissure, it is fair to assume that complete removal of the primary lesion could have been secured by laryngectomy.

Subglottic carcinoma is diagnosed late as symptoms commonly do not manifest themselves until the lesion has extended to the vocal cords. In my earlier cases I believed that removal by laryngofissure was adequate. Subsequent developments have indicated conclusively that a more extensive removal should be carried out and in questionable cases a prophylactic block dissection of the neck be part of the primary operation. I agree with Orton that subglottic carcinoma of the larynx is best treated by laryngectomy.

Carcinoma of the epiglottis commonly begins near its base. It rarely is observed as a marginal lesion. These lesions too are commonly advanced before a diagnosis is made since the vocal cords practically never are involved, symptoms are meager and the lesion often is overlooked even by laryngologists. There is a tendency for direct invasion of the pre-epiglottic space as the lymphatic drainage from the base of the epiglottis and the anterior extremity of the ventricular band is carried

across this space through the thyrohyoid membrane (4). Conservative treatment therefore is inadequate and laryngectomy as recommended by Bísí gives the best results.

Roentgen studies of the neck particularly lateral views and tomograms are of value to ascertain the extent of carcinoma, particularly in those cases in which one cannot visualize the substenotic portion of the growth. In order to have a soft tissue shadow appear on a roentgen film so that it can be recognized as abnormal, it must be of considerable size and, unfortunately, in a diagnosis of carcinoma, lesions of considerable size commonly are advanced. It is important that diagnostic aids be accorded their proper value. Mirror laryngoscopy with or without direct examination still is the best method to ascertain the location and extent of a lesion in the larynx.

On the basis of extent and location of the carcinoma I believe that all lesions confined to the larynx with the exception of those involving the anterior and middle thirds of a vocal cord without extension to the opposite side and without fixation of the cord should be treated by laryngectomy.

Fixation of an arytenoid indicates involvement of the cricoarytenoid joint and extension to the posterior or larynx. Fixation of a vocal cord is observed when there is infiltration of its musculature by carcinoma. This is a significant sign and should suggest that conservative surgery probably will be inadequate.

While the grade of malignancy of a carcinoma should be considered in the selection of treatment I do not believe that it is as important as the foregoing. A majority of vocal cord and epiglottic tumors are of a low or intermediate grade of malignancy, and undifferentiated carcinoma is not commonly observed. On the other hand carcinoma of a ventricular band or arytenoid frequently is undifferentiated in type.

Metastasis and extralaryngeal extension seriously influence the plan of therapy and the prognosis. I believe, however, it has been conclusively shown that the outlook is better if radical surgery is resorted to. Pre-epiglottic extension of carcinoma of the epiglottis has been successfully treated with radical surgical removal of the pre-epiglottic space and laryngectomy. I consider this type of case far more favorable for surgical treatment than a primary lesion in the pyriform sinus or in the interarytenoid area where metastases occur early. Metastasis to the deep cervical lymph nodes in the region of the bifurcation of the carotid artery complicating carcinoma of a vocal cord or epiglottis does not constitute a hopeless problem, and better results can be secured by block dissection and laryngectomy than by laryngectomy plus irradiation. For a time I performed laryngectomy and block dissection as separate procedures. Since 1942 this has been done as a one stage procedure and in the first patient treated in this manner there has been no recurrence for more than 5½ years. I have done this operation a number of times since with excellent immediate postoperative results as well as nonrecurrence of carcinoma although the customary 5 years have not elapsed. I believe therefore that the outlook of carcinoma of the larynx from a surgical standpoint is good. I further believe that if laryngectomy is performed more often in preference to conservative surgical treatment in the borderline cases there will be fewer recurrences. In cases with metastasis radical resection of the entire area together with removal of the primary lesion can be carried out with safety and the results will be far better than those secured by any other method or combination of methods.

Laryngectomy has been described as a formidable, mutilating operation which leaves the patient an economic burden and a psychologic wreck. In discussing the psychology of laryngectomized patients, Schall found them a cheerful and optimistic group who readily make readjustments. This has been the usual experience. A large number of these patients can be taught to talk and the remaining group can have recourse to mechanical or electrical devices. I have had but one patient who failed to adjust himself and regretted his decision to have a laryngectomy. This phase of the problem therefore should not be considered as a factor when determining the plan of treatment.

TECHNIQUE

The fundamental principles underlying the technique of laryngectomy remain unchanged.

The choice of anesthetics must be left to the individual operator. I prefer local anesthesia by infiltration supplemented by barbiturates for laryngectomy. In case block dissection and laryngectomy are required, inhalation anesthesia, preferably by intubation, is desirable. Variations in the technique of laryngectomy are necessary to meet certain requirements. Thyrotomy should be done if there is a question concerning laryngofissure or laryngectomy. Conservation of structures about the larynx notably attachment of muscles has I believe certain hazards and violates one of the primary principles of the surgical treatment of cancer. There is nothing to be gained by saving muscular attachments or even the ribbon muscles, and there always is a chance of retaining tissues that are the seat of metastatic carcinoma, notably in the pretracheal region. I therefore remove all of these routinely. In addition, a segment of hyoid bone is removed routinely. In invasion of the pre-epiglottic space the entire hyoid bone and the pre-epiglottic space are removed intact.

For a time I employed the Barretto clamp but have discontinued this during the past 16 months (8). My objection to it is that it prevents visualization of the lesion during the removal of the larynx and also requires that the trachea be amputated early in the operation since the larynx must be removed from below upward. I prefer to remove the larynx from above downward so that I can more clearly visualize the lesion; in addition, it lessens the hazards of aspiration of blood into the trachea. Since discontinuing the use of the clamp I have employed a technique which protects the wound from pharyngeal contamination and retains the laryngotracheal airway until near the completion of the operation. After the larynx is skeletonized and the mucosa of the epiglottis is freed along its lingual aspect, a No. 0 nontraumatic chromic suture is passed through the mucosa and fascia between the base of the tongue and the epiglottis (Fig. 2). When this suture is tied, the pharynx is opened and, with the suture held taut, it is possible to prevent contamination of the wound by secretions (Fig. 3). This procedure permits one to inspect the lesion particularly if there is a question of extension laterally which often cannot be satisfactorily visualized in extensive lesions by mirror or direct laryngoscopy. Suturing of the mucosa of the pharynx can be carried out as its separation from the larynx proceeds so that at no time is there any danger of spilling over of secretions (Fig. 4). In addition the airway is protected and there is no aspiration of blood or mucus. Complete skeletonization of the larynx can be completed, the second layer of sutures corresponding to the pharyngeal constrictors can be placed, and drainage tubes through an independent counter opening can be inserted before the larynx is amputated. If there is dyspnea a Flagg tube may be inserted at any time.

In subglottic extension, particularly when there is stenosis of the larynx which cannot be traversed by direct laryngoscopy, it is difficult to determine the level of amputation. To ascertain if the growth extends subglottically, I employ a laryngeal mirror through the opening made between the cricoid cartilage and the first tracheal ring to secure a reflected image of the subglottic larynx. This has been helpful in many instances to determine whether the line of amputation should be continued at that level or whether one should remove one or more additional tracheal rings. When growths extend down to the level of the first tracheal ring the prognosis usually is hopeless because of metastasis along the party wall.

MORTALITY RATE

The postoperative mortality of laryngectomy is low and with antibiotics, pulmonary complications are uncommon and primary healing is the rule. The most common cause of postoperative mortality is cardiovascular complications. In 326 cases of laryngectomy there was a postoperative mortality of 14 (4.3 per cent). Of these, 6 died from pulmonary complications and 8 from coronary occlusions, cardiorenal disorders or apoplexy.

RESULTS

It is difficult to evaluate end-results following laryngectomy unless one classifies cases according to anatomical location and extent of involvement. If the carcinoma is confined to the larynx and there is no metastasis to

lymph nodes, then the 5 year nonrecurrence rate following laryngectomy should be 100 per cent. A local recurrence indicates that the procedure was inadequate. An inadequate procedure is the common cause of failure following laryngofissure or irradiation. The common causes of failure following laryngectomy are regional and distant metastases.

In carcinoma involving the anterior commissure or the base of the epiglottis without extension to the pre-epiglottic space a 5 year nonrecurrence rate of at least 90 per cent can be obtained by laryngectomy. With increasing invasion of carcinoma in these sites, the rate declines and ultimately is under 50 per cent.

Subglottic carcinoma carries a high mortality rate since metastasis occurs to the lower nodes of the cervical chain and along the party wall. Both areas are inaccessible surgically.

Carcinoma of a ventricular band, aryepiglottic fold or arytenoid usually gives a poor result for it often is discovered late, commonly is undifferentiated in type, and metastasizes early.

CONCLUSION

At the present time the best results in the treatment of uncomplicated carcinoma of the larynx are secured by surgical extirpation. Surgical extirpation implies a procedure sufficiently radical to remove the entire primary lesion. One cannot be swayed by emotional or economic considerations. To save the voice may result in loss of life. There must be but one real objective, and patients too can appreciate the need for this. Conservation of portions of cartilage, muscles, or their attachments for cosmetic or functional betterment is unsurgical and unsafe in the treatment of carcinoma of the larynx.

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THE EFFECT OF ABSORBABLE SPONGE MATERIALS ON THE ACTIVITY OF THROMBIN

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SINCE the isolation of thrombin for practical use by Seegers and his associates in 1938 (18, 19, 22) the interest in absorbable hemostatic agents has rapidly increased. The war lent impetus to the search for an "absorbable sponge" that might give the added advantage of the pressure factor in the control of hemorrhage difficulty checked by ligature or the topical application of thrombin.

Of these absorbable sponge materials developed in recent years the 3 receiving the most study have been cellulose oxidized by nitrogen dioxide, gelatin, and "fibrin foam" obtained by fractionation of human plasma.

Since these materials followed closely on the heels of thrombin and since thrombin is itself the most active clotter of blood or plasma known at the present time, it is natural that they should be used clinically in conjunction with thrombin. They have also been used very effectively as hemostatic agents without the use of thrombin, particularly oxidized cellulose and gelatin. This paper deals with the relationship of these three materials to thrombin.

Oxidized cellulose. Yackel and Kenyon in 1942 reported the development of an oxidized cellulose which was readily soluble in dilute alkalies and which even with a high degree of oxidation remained fibrous and not friable. The degree of oxidation, depending on the content of the carboxyl groups, was readily controlled and hence the end product might be varied according to the need for a more or less soluble, absorbable, or pliable substance. Material containing less than 15 per cent carboxyl groups is not brittle and is easily handled without breaking up. It is slightly degraded by oxidation and may change from its original white to an off white. It does not stand autoclaving, but may be satisfactorily sterilized by formaldehyde. It withstands boiling for 3 minutes.

Frantz (6) placed oxidized cellulose in muscle, brain, dura, joint, and peritoneum of animals and found a minimum of tissue reaction. Absorption of the material varied between 10 days and 6 weeks, being complete in all cases at the end of this time. The tissue reaction was more marked in the case of the more highly oxidized cellulose, apparently because of the higher carboxyl content. In 2 instances the cellulose was soaked in thrombin before being buried in the brain, and in these cases the tissue reaction was less than when the cellulose was used alone. Putnam found soluble cellulose dampened with thrombin an effective hemostatic agent. Cronkite, Deaver and Lozner used oxidized cellulose with thrombin of both rabbit and human origin and found it effective as a hemostatic agent in both traumatic and elective surgery.

In 1944 Seegers and Doub (20) showed that oxidized cellulose having a carboxyl content of 14 per cent rapidly reduced the *p*H of a standardized thrombin solution to below 4.3, the inactivation point of thrombin. They further showed that when this same cellulose was first soaked in a 1 per cent solution of bicarbonate of soda for a sufficient period of time the *p*H of the thrombin remained on the alkaline side and its activity was unaltered. They also found that when the oxidation of cellulose is carried further than is required for rapid absorption *in vivo*, acidity remains a factor, but there are other products of oxidation which destroy thrombin. Cellulose having a carboxyl content of 21 per cent when first soaked in a 1 per cent solution of sodium bicarbonate did not alter the *p*H of thrombin, but its activity when tested against a standardized fibrinogen solution had disappeared. The nature of the destruction is unknown.

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Frantz, Clarke, and Lattes (8) made some interesting observations on the physical changes of cellulose in the wound. The material when dry was easily packed into a wound, and when saturated with blood turned dark brown and seemed to swell, thus expanding into the crevices of the wound. There seemed to be an affinity of the gauze for certain of the blood elements. This tendency was further demonstrated when oxidized cellulose was added to a test tube containing dilute, hemolyzed blood. The blood cleared rapidly and the cellulose turned a dark brown, the hemoglobin apparently combining in some way with the cellulose. (Yackel and Kenyon found oxidized cellulose to have an affinity for basic dyes, and it is possible that that quality is represented in this instance.) These characteristics of the cellulose disappeared when the material was first neutralized by calcium acetate, and it was less effective as a hemostatic. These authors suggest, then, that the oxidized cellulose when used dry has hemostatic properties of its own, and that its combination with thrombin may be unnecessary and even undesirable.

Uihlein, Clagett, Osterberg, and Bennett made some interesting observations on the effect of certain solvents on oxidized cellulose. In plain water or normal saline it was half destroyed by the third day. In 5 per cent solution of sodium bicarbonate it disappeared in 20 minutes. In 10 per cent formalin, cellulose residue was difficult to identify at the end of the third day. In 70 per cent alcohol it became somewhat fluffy and soft, and in 95 per cent alcohol it underwent no change. When kept in pooled serum or whole blood at room temperature, it disappeared in 7 days. Cellulose left in wounds was absorbed at the end of 4½ days. When they used it in wounds with thrombin, hemostasis was excellent in 37 cases and satisfactory in 20 cases. In a few instances in which it was used without thrombin, hemostasis was excellent. When it is used with thrombin they recommend it first be dipped in a 1 per cent solution of sodium bicarbonate to which has been added an antiseptic, a 1:5000 solution of phemerol.

Recently Frantz and Lattes (9) have suggested that the dry cellulose affords a hemostatic effect by the formation of coagula consisting of salts of cellulosic acid and hemoglobin. They suggest also that this makes the addition of thrombin superfluous and that the acidity of the cellulose may inactivate the thrombin. They found that the dry cellulose when placed in bone in clean experimental fractures delayed the formation of callus, though when the gauze was removed from a compound fracture site after a few days there was no significant delay in the healing of the fracture. Frantz (7) reports the unpublished work of Kabat, Hennig, and Victor in which they injected the sodium salt of cellulose intravenously in rabbits. They found it was rapidly eliminated in the urine without breakdown, and its rate of disappearance from the blood and excretion in the urine could be measured using precipitation tests with types III and VIII antipneumococcus serum. In this connection Heidelberger and Hobby found that oxidized cellulose by virtue of its cellubiuronic acid content will precipitate antipneumococcus types III and VIII horse sera, suggesting possible immunological properties of the cellulose.

Fibrin foam. In 1915 Grey used fibrin as a hemostatic agent. Pieces of washed, autoclaved sheep fibrin measuring 3½ by 2 by 1½ centimeters were completely absorbed in the brains of cats after 6 weeks with a minimal amount of tissue reaction. They caused less reaction than similar implants of muscle. The following year Harvey made fibrin film by grinding fibrin into fine bits and compressing it into a thin sheet. Pieces 40 micra in thickness were absorbed in animal tissues in 2 weeks. Cushing successfully used such film as a hemostatic in cerebral surgery.

In 1944 Bering reported the development of "fibrin foam" through the fractionation of human plasma. In the dry state this material is a porous mass of fibrin fibers between which there are microscopic and macroscopic air spaces. It appears as a homogeneous, dull, rough, slightly brittle mass. When placed in an aqueous solution, the latter penetrates the multiple channels and the foam loses its brittleness, becomes compressible, slightly resilient, and, when entirely wet, shows some shrinkage. By varying the proportions of the two essential proteins, thrombin and fibrino-

gen, and the conditions under which they are processed, a wide range of products may be obtained. At one extreme is the light fluffy foam that shrinks when wet to about 10 per cent of its dry volume. At the other extreme is a dense, firm substance which shrinks only about 50 per cent when wet. Variations in elasticity and flexibility are also possible with variations in physical and chemical treatment. By varying the procedure of production a wide range of thrombic activity may be obtained, thus providing for use as a hemostatic alone or in conjunction with a thrombin solution. The material may also be produced with varying fibrinolysin content and varying susceptibility to bacterial fibrinolysin so that its rate of absorption *in vivo* and *in vitro* may be controlled. The material so produced is sterile and does not stand boiling or autoclaving without change of mechanical properties. Bailey and Ingraham (1) implanted fibrin foam and oxidized cellulose soaked in thrombin under the dura of monkeys. They later found adhesions between the dura and arachnoid on the side in which the cellulose was placed. They found no difference in the degree of tissue reaction or the rate of absorption between the two substances.

Bailey and his associates (2) implanted fibrin foam and soluble cellulose, both materials with and without thrombin, in the liver, peritoneal cavity, abdominal wall, kidney and lung of experimental animals. In all instances there was minimal tissue reaction and little difference in that elicited by the two substances. Both were absorbed in 5 weeks or less, the cellulose disappearing in a slightly shorter time than the fibrin foam. The hemostatic effect was satisfactory in all instances. In 240 general surgical cases fibrin foam and thrombin were effectively used as hemostatic agents.

Gelatin sponge. In 1945 Correll and Wise (3) reported the preparation of an absorbable water-insoluble gelatin-base sponge obtained by foaming a gelatin solution and drying it in special forms. It is white, tough, porous, nonelastic and may be cut into any desired size or shape. It will take on 50 times its weight of water and about 45 times its weight of blood. It was found to be nonantigenic.

Correll, Prentice, and Wise (4) placed implants of gelatin sponge, fibrin foam and starch, each soaked in thrombin, into the muscles of rats. Each elicited a minimal tissue reaction. They found the gelatin sponge completely absorbed in 30 days, starch persisted through the 50th day after implantation, and fibrin foam was not completely absorbed at the 100th day. Light and Prentice made similar comparisons on thrombin soaked implants of gelatin and fibrin foam placed deep into the brain, subcortically, subdurally, and as patches to repair torn venous sinuses. They found no appreciable difference in tissue reaction to the two types of sponge when implanted under similar conditions. Neither was there any difference in tissue reaction when human thrombin was substituted for the bovine product. Both the gelatin and fibrin foam patches effectively stopped the flow of blood from a torn venous sinus, and there was no instance of a thrombus occuring in the sinus channel.

Gelatin sponges without thrombin were implanted into various animal tissue by Jenkins and Clarke (13). The tissue reaction was less than that elicited by cat gut, and the material was absorbed in about 5 weeks. They found it to be an efficient hemostatic in its own right. Jenkins, Janda and Clarke (14) used it experimentally with and without thrombin and report a more rapid hemostasis when thrombin was used. The difference, however, was not marked. In comparing gelatin sponge with fibrin foam and oxidized cellulose, they found the immediate hemostatic efficiency of the three about equal. The soluble cellulose, however, did not adhere so firmly to the tissue surface as did the gelatin, and the fibrin foam was more easily broken up. Jenkins and Janda (15) made stab wounds in the large veins including the vena cava in dogs, and in other instances excised a portion of the vein wall. They used gelatin sponge without thrombin as patches to cover the defects. In most instances the hemostasis was successful and the defects were closed by an endothelialized scar at the end of 3 weeks. After a month it was difficult to identify the sponge grossly. Again they demonstrated that gelatin sponge alone is an effective hemostatic agent, though they

TABLE I.—EFFECT OF OXIDIZED CELLULOSE ON THE ACTIVITY OF BOVINE AND HUMAN THROMBIN

Substance	*p*H	Clotting time (seconds) after addition of 0.1 c.c. thrombin solution		Hour
		Oxalated plasma, 0.1 c.c.	1% Fibrinogen solution, 0.1 c.c.	
Distilled water 60 c.c.	6.05			
Plus thrombin (bovine) 5000 units	7.04		4.2	9:25
			3.0	
			4.6	
Plus cellulose 0.112 gm.	4.81	4.4	4.1	10:15
		4.6	4.0	
Plus cellulose 0.112 gm. (total 0.224 gm.)	3.67	No clot after 3 minutes	No clot after 3 minutes	10:30

The *p*H of the thrombin is rapidly reduced to below its inactivation point on the addition of a total of 0.224 gm. of oxidized cellulose, about 1/5 the amount packaged by the manufacturer. Note that the thrombin is still active after 0.112 gm. of cellulose has been added, and the *p*H is still above the inactivation level of thrombin. The amount of cellulose is less than that likely to be used clinically for hemostasis in most instances. The compatibility of smaller amounts of cellulose and larger unitages of thrombin was not investigated.

TABLE II.—EFFECT OF OXIDIZED CELLULOSE ON THE ACTIVITY OF BOVINE AND HUMAN THROMBIN

Substance	*p*H	Clotting time (seconds) after addition of 0.1 c.c. thrombin solution		Hour
		Oxalated plasma, 0.1 c.c.	1% Fibrinogen solution, 0.1 c.c.	
Normal saline 60 c.c.	5.89			
Plus thrombin (human) 200 units	6.92	17.2	8.7	12:15
		16.4	8.2	
Plus cellulose 0.275 gm.	4.57	64.9	No clot after 3 minutes	12:30
		76.8		
Plus cellulose 0.275 gm. (total 0.550 gm.)	3.06	No clot after 3 minutes	No clot after 3 minutes	12:45

In this instance the *p*H of the thrombin solution was reduced to below its point of inactivation after the addition of 0.550 gm. of cellulose.

believe that the addition of thrombin enhances and accelerates the hemostatic action.

EXPERIMENTAL STUDY

In view of the increasing use of absorbable sponge materials, in many instances in conjunction with thrombin, it seemed of interest and importance to investigate the effects of the various substances on the activity of thrombin. Included in this study are absorbable cellulose, fibrin foam, and gelatin used with human and bovine thrombin as described below. Quantities of each substance were in general kept within limits likely to be used clinically for hemostasis. No attempt was made to investigate the extreme limits of compatibility of the substances.

Thrombin, human and bovine, in varying unitages was dissolved in both distilled water and normal saline solution. The *p*H of each solvent was measured by means of the glass electrode before and after the addition of the thrombin and at various stages after the addition of the soluble sponge material. The activity of the various thrombin solutions was determined by adding 0.1 cubic centimeter of the particular solution to 0.1 cubic centimeter of standardized fibrinogen solution and checking the clotting time. Similar tests were made in each instance, freshly collected oxalated human plasma being used in the same quantities. The prothrombin in the plasma was rendered inactive by the oxalate, but the fibrinogen was still available for reaction with thrombin.

Various absorbable sponge materials in weighed amounts were added to the respective thrombin solutions and the *p*H and activity of the solutions measured after each such addition. The time factor was also taken into account. As a rule, sponge samples were added until there was little or no further change in the *p*H of the thrombin solution, and in many instances no further change in the activity of the thrombin. Most experiments were completed within a 2 hour period, though in a number of instances the thrombin, when its activity was little affected by the sponge, was stored at approximately 5 degrees centigrade, and its activity followed at intervals for as long as 47 days. No attempt was made to keep the solutions sterile.

In the case of oxidized cellulose various reagents were used in an attempt to neutralize its acid character, among these being sodium bicarbonate, sodium oxalate, sodium citrate, sodium acetate, imidazole and glycerin. The cellulose was soaked in these solutions for varying periods of time before being placed in the thrombin solution.

TABLE III.—EFFECT OF BUFFERING ACTION OF 1 PER CENT BICARBONATE OF SODA ON THE ACID NATURE OF OXIDIZED CELLULOSE

Substance	*p*H	Clotting time (seconds) after addition of 0.1 c.c. thrombin solution		Hour
		Oxalated plasma, 0.1 c.c.	1% Fibrinogen solution, 0.1 c.c.	
Normal saline 60 c.c.	5.89			
Plus thrombin (human) 200 units	6.46	13.4	9.3	10:00
		12.9	9.0	
			9.9	
Plus cellulose 0.277 gm.	4.04	55.9	35.6	10:15
		48.5	39.2	
		56.9	37.7	
Plus cellulose 0.280 gm.	3.51	91.8	No clot after 3 minutes	10:30
		81.1		
Plus cellulose 0.282 gm. (total 0.839 gm.)	3.38	No clot after 3 minutes		10:45

Each sample of cellulose was soaked for 1 minute in a 1 per cent solution of bicarbonate of soda before being added to the thrombin solution. Note that though considerably delayed, clotting of the plasma does take place after the *p*H of the thrombin has dropped to 3.51, well below the point of inactivation of thrombin. This would indicate that the inactivation is not immediately irreversible and as shown here the natural buffering action of the plasma has been sufficient to raise the *p*H to a point where some activity of the thrombin has been restored. The fibrinogen solution is not buffered hence the thrombin solution remains inactive on contact with it.

TABLE IV.—EFFECT OF BUFFERING ACTION OF 1 PER CENT BICARBONATE OF SODA ON THE ACID NATURE OF OXIDIZED CELLULOSE

Substance	*p*H	Clotting time (seconds) after addition of 0.1 c.c. thrombin solution		Hour
		Oxalated plasma, 0.1 c.c.	1% Fibrinogen solution, 0.1 c.c.	
Distilled water 60 c.c.	6.39			
Plus thrombin (bovine) 5000 units	7.23	2.4	3.5	10:15
		2.5	2.6	
Plus cellulose 0.274 gm.	5.71		5.2	10:30
			6.2	
Plus cellulose 0.278 gm.	5.13	6.2	13.8	10:40
		5.8	15.4	
Plus cellulose 0.278 gm. (total 0.830 gm.)	4.85	6.4	30.8	10:50
		6.8	32.7	
	4.54	17.4	34.3	11:20
		17.4	34.6	
	4.51	21.4	31.5	11:45
		22.6	33.1	

Each sample of cellulose was soaked for one minute in a 1 per cent bicarbonate of soda solution before being added to the thrombin solution. The *p*H of the thrombin solution was reduced by the buffered cellulose but still active after the addition of 0.830 gm. of the material.

RESULTS

Oxidized cellulose in small amounts, when added to thrombin solutions of varying strengths and volumes, reduced the *p*H to the inactivation level or below within a few minutes. These thrombin solutions were highly active before the addition of the cellulose and became inactive when the *p*H dropped to below 4.3. This was true in the case of both the bovine and human thrombin and when put into solutions of either distilled water or normal saline. Typical reactions are shown in Tables I and II. If cellulose was first soaked in a 1 per cent solution of sodium bicarbonate for 30 seconds before being added to the thrombin solution, similar results were obtained. The *p*H of the thrombin dropped rapidly and the thrombin became inactive. When this buffering time was increased to one minute, there were varying effects. In all instances there was a lowering of the *p*H value of the thrombin but usually not below its point of inactivation. In other instances the *p*H dropped to below this point. The activity of the thrombin was diminished in all instances and followed in degree for the most part the *p*H values. Tables III and IV show two representative reactions. Leaving the cellulose in the buffering solution longer (total of 5 minutes) materially slowed the reduction in *p*H of the thrombin solution, but the activity of the latter was still reduced (Table V). This supports the work of Seegers and Doub (20) who found an unexplained factor, other than a reduction of the *p*H value, by which cellulose having a carboxyl content of 21 per cent interfered with the activity of thrombin. The cellulose in this study had a carboxyl content of 18.5 per cent.

However, oxidized cellulose soaked in the 1 per cent bicarbonate solution for as short a time as 1 minute began to disintegrate and was not well suited to packing into a wound. It assumed an amorphous, jellylike mass that broke up with handling. Dissolving the dry thrombin in a 1 per cent solution of sodium bicarbonate achieved the desired buffering effect, but the oxidized cellulose soaked in it

TABLE V.—EFFECT OF ADEQUATELY BUFFERED CELLULOSE ON THE ACTIVITY OF THROMBIN

Substance	*p*H	Clotting time (seconds) after addition of 0.1 c.c. thrombin solution		Hour
		Oxalated plasma, 0.1 c.c.	1% Fibrinogen solution, 0.1 c.c.	
Distilled water 60 c.c.	6.05			
Plus thrombin (bovine) 5000 units	6.92	3.0	2.6	9:15
		3.2	2.4	
Plus cellulose 0.278 gm.	7.2	10.0	13.0	9:30
		11.0	9.8	
			10.2	
Plus cellulose 0.274 gm.	7.2	20.0	14.0	9:50
		21.2	14.2	
			15.0	
Plus cellulose 0.278 gm.	6.90	29.8	28.0	10:20
		30.2	27.2	
		30.0	30.4	
Plus cellulose 0.280 gm. (total 1.110 gm.)		No clot after 3 minutes	No clot after 3 minutes	11:00

Each sample of cellulose was soaked in a 1 per cent solution of bicarbonate of soda for 5 minutes before being added to the thrombin solution. The cellulose was adequately buffered in this instance and the *p*H of the thrombin solution little affected. Despite this the activity of the thrombin declined and finally disappeared after the addition of 1.110 gm. of cellulose. This supports the work of Seegers and Doub (20) who found an unexplained factor, other than a reduction of the *p*H value, by which cellulose having a carboxyl content of 21 per cent interfered with the activity of thrombin. The cellulose used in this instance had a carboxyl content of 18.5 per cent.

rapidly assumed the same jellylike consistency, and was poorly suited to packing.

In an attempt to find another buffer that would not so readily dissolve the cellulose, samples of the material were added to solutions of sodium citrate, sodium oxalate, sodium acetate and glycerin. The buffering action of the citrate was about the same as that of the bicarbonate, and that of the oxalate, acetate and glycerin considerably less. In all instances, however, the cellulose began to dissolve within 3 minutes of the time it was added to the buffer. Imidazole, a buffer used successfully in certain processes involving blood clotting because it does not precipitate calcium salts, was investigated. Its buffering qualities were better than those of any of the above substances, but the cellulose dissolved as rapidly in it as in the other solutions.

Fibrin foam. When fibrin foam was added to a solution of human thrombin in distilled water or normal saline, there was a slight lowering of the *p*H value of the thrombin (Tables VI and VII). The activity was also slightly reduced though the change in both the *p*H and thrombic action was so minimal as to be of no clinical significance. As more fibrin foam was added to the same thrombin solution, the *p*H was further lowered and the thrombic activity changed accordingly. The changes after the addition of up to twice the amount usually packaged with one thrombin sample were still so slight as not to impair materially the usefulness of the solution clinically. If such solutions of thrombin were stored at 5 degrees centigrade with the fibrin foam still present in the solution, the thrombic activity remained little changed for from 8 to 12 days. After that, though the *p*H values were not further lowered, but in fact came up slightly, the thrombic activity continued to decline. One sample which clotted the fibrinogen solution at 6.4 seconds originally gave a clotting time of 33 seconds after 37 days (Table VII). This represents a fair degree of thrombic activity. Plasma that was originally clotted at 9.5 seconds by the same thrombin solution gave an average clotting time of 21 seconds after the thrombin had been stored for 38 days (Table VII). This apparent higher degree of activity of the fibrinogen in the plasma may be on the basis of the buffering action of the plasma. The fibrinogen solution did not contain a buffer.

Gelatin sponge. When gelatin sponge was added to bovine thrombin in either normal saline or distilled water, the *p*H value of the solution was lowered. This occurred to a greater degree than when fibrin foam was added to thrombin, but the *p*H level in all instances in this study was well above the inactivation point of thrombin. Even though the gelatin reduced the *p*H of thrombin more than did the fibrin foam, the resulting thrombic activity was much the same. Tables VIII and IX are representative of the changes in *p*H values and thrombic action when gelatin sponge is added to thrombin solution. When stored at 5 degrees centigrade with the gelatin still in the solution of thrombin, the activity of that solution remained fairly uniform over a period of 4 to 17 days with an average of 13 days. In

TABLE VI.—EFFECT OF FIBRIN FOAM ON THE ACTIVITY OF THROMBIN

Substance	pH	Clotting time (seconds) after addition of 0.1 c.c. thrombin solution		Hour	Date
		Oxalated plasma, 0.1 c.c.	1% Fibrinogen solution, 0.1 c.c.		
Normal saline 20 c.c.	6.27				10–1–46
Plus thrombin (human) 200 units	7.06	9.2	5.0	11:15	
		9.4	5.2		
Plus fibrin foam 0.045 gm.	6.67		6.0	11:35	
			5.8		
Plus fibrin foam 0.08 gm.	6.57		7.4	11:40	
			7.6		
Plus fibrin foam 0.09 gm.	6.54		9.4	11:50	
			8.8		
			8.4		
Plus fibrin foam 0.34 gm. (total 0.555 gm.)	6.43	19.8	14.1	12:05	
		17.6	13.8		
			13.6		
	6.43		15.2	12:20	
			16.2		
			16.4		
	6.42		16.2	10:00	10–2–46
			16.0		
			16.8		
			14.8	10:15	10–4–46
			16.6		
			16.8	9:00	10–5–46
			17.4		
			16.6		
			19.8	8:45	10–8–46
			18.4		
			17.8		
		13.2	14.8	11:15	10–12–46
		11.8	14.6		
		16.8	25.6	10:30	10–14–46
		14.2	25.2		
		12.4	46.2	11:00	10–16–46
			45.9		
		11.2	28.6	11:00	10–18–46
		10.4	29.4		
	7.09	16.2	24.4	9:00	10–22–46
		16.8	21.0		
	7.45	14.8	23.3	9:00	10–24–46
	Q.N.S.	15.8	18.4	9:00	10–26–46
		16.1	19.2		
		13.1	21.2	10:00	10–29–46
		12.8	21.8		
		18.5	38.4	10:00	10–31–46
		18.8	42.0		
		22.8	37.3	10:00	11– 8–46
		24.1	38.1		
		25.4	26.4	10:00	11–10–46
		25.1	25.8		

The pH of the thrombin was slightly reduced by the addition of fibrin foam, but after the addition of a total of 0.555 gm. of the latter, a fair degree of thrombin activity remained for as long as 36 days.

TABLE VII.—EFFECT OF FIBRIN FOAM ON THE ACTIVITY OF THROMBIN

Substance	pH	Clotting time (seconds) after addition of 0.1 c.c. thrombin solution		Hour	Date
		Oxalated plasma, 0.1 c.c.	1% Fibrinogen solution 0.1 c.c.		
Distilled water 20 c.c.	5.94				9–23–46
Plus thrombin (human) 200 units	7.11		6.8	9:25	
			6.4		
			6.0		
Plus fibrin foam 0.065 gm.	6.97	9.4	7.6	9:50	
		9.6	7.8		
Plus fibrin foam 0.070 gm.	6.91		7.2	10:05	
			6.4		
			7.0		
Plus fibrin foam 0.090 gm.	6.86	11.8	9.4	10:25	
		11.6	9.2		
			8.4		
Plus fibrin foam 0.055 gm. (total 0.28 gm.)	6.81		9.2	10:40	
			8.8		
			8.2		
	6.81		8.0	11:15	
			8.8		
			8.4		
	6.82	13.4	8.2	11:45	
		12.6	8.4		
			8.6		
	6.80	13.2	8.4	11:10	9–24–46
			8.4		
	6.56		9.4	11:05	9–27–46
			9.2		
			8.6		
	6.51		9.4	8:45	9–28–46
			9.6		
		12.2	10.8	10:45	9–30–46
		12.0	12.1		
			10.2	10:00	10– 2–46
			10.8		
			11.2	10:15	10– 4–46
			10.6		
			12.0	9:00	10– 5–46
			11.6		
		11.4	17.2	11:15	10–12–46
		14.2	16.4		
		16.4	20.0	10:30	10–14–46
		16.0	19.6		
		11.6	25.2	11:00	10–16–46
		11.4	24.4		
		9.8	17.8	11:15	10–18–46
		10.2	18.2		
		22.2	22.8	9:15	10–22–46
		20.4	24.2		
	7.57	18.0	22.3	9:00	10–24–46
		18.9	21.6		
	Q.N.S	20.8	23.5	10:00	10–26–46
		21.4	22.8		
		14.4	21.5	10:00	10–29–46
		14.1	21.4		
		23.0	32.3	10:00	10–31–46
		18.8	33.6		

In this instance a total of 0.28 gm. of fibrin foam affected the pH of the thrombin slightly, and the thrombic activity was not greatly reduced after 38 days.

TABLE VIII.—EFFECT OF GELATIN SPONGE ON THE ACTIVITY OF THROMBIN

Substance	pH	Clotting time (seconds) after addition of 0.1 c.c. thrombin solution		Hour	Date
		Oxalated plasma, 0.1 c.c.	1% Fibrinogen solution, 0.1 c.c.		
Normal saline 60 c.c.	6.01				9–21–46
Plus thrombin (bovine) 1000 units	8.03		8.2	9:20	
			7.2		
			7.2		
Plus gelatin 0.270 gm.	6.27	10.8	7.4	9:45	
		9.4	7.6		
			7.8		
Plus gelatin 0.200 gm.	5.89		9.4	10:05	
			9.2		
			8.2		
Plus gelatin 0.125 gm.	5.54	11.4	9.4	10:25	
		10.6	9.2		
			9.2		
Plus gelatin 0.115 gm. (total 0.710 gm.)	5.44		10.2	10:45	
			10.6		
			10.0		
	5.42	18.0	10.4	11:15	
		16.4	10.6		
	5.44		11.2	11:45	
			11.0		
			11.4		
	5.54	11.2	10.2	11:10	9–23–46
			11.4		
	5.46	10.8	10.8	11:00	9–24–46
			10.0		
	5.47		11.8	11:00	9–27–46
			11.6		
	5.46		12.2	8:40	9–28–46
			13.0		
			12.8		
	5.42	10.6	11.8	10:40	9–30–46
		11.0	12.6		
Gelatin dissolved			10.4	10:00	10– 2–46
			11.8		
			14.0		
			11.2	10:15	10– 4–46
			10.6		
			13.4	9:00	10– 5–46
			13.8		
	6.88	26.2	30.6	11:15	10–12–46
		30.4	43.2		

The gelatin (0.710 gm.) reduced the pH of the thrombin to a greater degree than did the fibrin foam, but the activity of the thrombin was not materially affected after 14 days.

TABLE IX.—EFFECT OF GELATIN SPONGE ON THE ACTIVITY OF THROMBIN

Substance	pH	Clotting time (seconds) after addition of 0.1 c.c. thrombin solution		Hour	Date
		Oxalated plasma, 0.1 c.c.	1% Fibrinogen solution, 0.1 c.c.		
Normal saline 60 c.c.	5.74				9–20–46
Plus thrombin (bovine) 1000 units	8.04		7.6	9:45	
			7.8		
Plus gelatin 0.125 gm.	7.04	11.4	7.2	9:55	
		10.8	7.0		
Plus gelatin 0.12 gm.	6.16	11.8	8.0	10:08	
		11.4	8.2		
			8.0		
Plus gelatin 0.115 gm.	5.89	11.6	9.0	10:25	
			9.2		
			9.2		
Plus gelatin 0.125 gm. (total 0.485 gm.)	5.37	9.2	10.8	10:40	
		9.4	10.6		
			12.2		
			14.8		
	5.37		13.4	10:55	
			14.2		
			14.6		
	5.32	16.2	14.8	11:45	
		17.2	12.8		
		15.8	12.6		
	5.33	14.2	12.4	11:10	9–21–46
		15.0	17.2		
			13.4		
	5.39	16.8	13.8	11:00	9–23–46
		17.2	12.2		
	5.30	13.8	15.8	10:50	9–24–46
		14.2	16.8		
	5.32		24.8	10:55	9–27–46
			23.6		
	5.31		23.0	8:35	9–28–46
			22.4		
			23.6		
	5.32	17.8	24.2	10:15	9–30–46
		15.2	25.0		
			26.2	10:00	10 –2–46
			28.2		
			45.0	10:15	10– 4–46
			43.8		
			70.7	9:00	10– 5–46
			70.6		

In this instance 0.485 gm. of gelatin reduced the pH of thrombin to about the same degree as did 0.710 gm. (Table VIII), but the activity of the thrombin was reduced to a slightly greater degree in 12 days. In neither instance was the change of clinical significance.

most instances two to four times as much gelatin was added to the thrombin solution as is packaged with it by the manufacturers. Thus the possibility of any significant change in the activity of thrombin brought about by the usual amount of gelatin used is remote.

COMMENT

From this study it would appear that the use of thrombin with oxidized cellulose is a questionable procedure and may be contraindicated. Unbuffered cellulose in small amounts, by virtue of its acid nature, rapidly lowers the *p*H of thrombin and thus inactivates it. Cellulose may be properly buffered so that it does not alter the *p*H of thrombin to any great degree, but if the carboxyl content is sufficiently high, the thrombin is still inactivated by a factor in the cellulose as yet unknown.

Inasmuch as cellulose alone is a satisfactory hemostatic agent (8, 9, 17) and the acid nature of the material may be responsible for a certain degree of this hemostatic quality, it is likely that the thrombin by partially neutralizing it may impair its value as a hemostatic agent.

The finding by Frantz and Lattes (9) that dry cellulose placed at the site of a clean fracture delays the formation of callus would suggest that the unbuffered material should not be used in open fractures or in bone surgery where callus formation is desired. How much of a rôle the acid factor plays in the inhibition of callus formation and how much may be due to other factors is speculative. It is suggested that in conditions in which the formation of new bone is undesirable, as in fenestration of the wall of the inner ear and in certain arthroplasties, the use of cellulose might be of value in discouraging callus formation. It is suggested that variations in the percentage of carboxyl content of the cellulose might be of value in such conditions, thus providing different degrees of acidity and different absorption times of cellulose.

The use of buffering agents in our study was unsatisfactory because of the early disintegration of the cellulose in such solutions.

Fibrin foam and gelatin affected the activity of thrombin only slightly, and solutions containing these sponge materials remained active over a period of days. It is suggested that thrombin solutions made up for use in surgical procedures may be preserved at domestic refrigerator temperatures and in sterile condition for repeated use with fibrin foam and gelatin. Such solutions may be easily tested for thrombic activity by adding a few drops of the solution in question to a similar amount of citrated or oxalated blood. Such blood may be fresh or may be drawn from any bottle of bank blood suitable for transfusion. Blood not more than 3 weeks old should be satisfactory. The clotting of such thrombin-blood combinations in 25 seconds or less indicates a thrombic activity considerably greater than that of the normal spilled blood and satisfactory for clinical use.

SUMMARY AND CONCLUSIONS

1. Oxidized cellulose because of its extreme acid character rapidly reduces the *p*H of thrombin to below its point of inactivation—4.3.

2. This acid character may be neutralized by first soaking the cellulose in a buffering solution of 1 per cent bicarbonate of soda. In this study, soaking the cellulose for as short a time as 1 minute, minimum time required for such neutralization, resulted in a disintegration of the cellulose to such degree that it was poorly suited to packing into a wound.

3. Other buffering agents including sodium oxalate, sodium citrate, sodium acetate, glycerin and imidazole caused similar disintegration of cellulose. Thrombin dissolved directly in 1 per cent sodium bicarbonate gave similar results.

4. Oxidized cellulose having relatively high carboxyl content, properly buffered by bicarbonate of soda solution does not reduce the *p*H of thrombin materially, but the activity of the latter is still impaired by a factor as yet unknown.

5. Because of these factors the use of thrombin in conjunction with oxidized cellulose for hemostasis is considered a questionable procedure.

6. Fibrin foam when added to thrombin dissolved in either normal saline or distilled water reduced the *p*H of the thrombin slightly, but the reduction of neither the *p*H nor the throm-

bic activity was of sufficient degree to be of clinical significance. Such thrombin solutions when stored at 5 degrees centigrade retained sufficient activity for clinical use for an average period of 17 days, and in some instances showed a fair degree of activity after 38 days.

7. Gelatin sponge when added to thrombin solution diminished the *p*H of that solution to greater degree than did fibrin foam, though the thrombic activity was impaired to about the same degree. When stored at 5 degrees centigrade, samples of such thrombin solution remained sufficiently active for clinical use for an average period of 13 days, and in some instances were comparatively active after 37 days.

8. Solutions of thrombin made up for use at the operating table may be preserved at ordinary domestic refrigerator temperatures, in sterile condition and used over a period of days. The thrombic activity of such solutions is easily tested at the time of use by adding a small sample of it to citrated or oxalated blood.

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OPPONENS TRANSPLANT: AN ANALYSIS OF THE METHODS EMPLOYED AND RESULTS OBTAINED IN SEVENTY-FIVE CASES

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THE opposable thumb constitutes one of man's most useful attributes. It is, then, of utmost importance to consider means of restoring opposition to thumbs deprived of it by injury to nerves or by direct loss of muscle.

It is the purpose of this paper to review our experience with tendon transfer for restoration of opposition in 84 cases of wounds of the upper extremities incurred in World War II, in 75 of which sufficient data were available to permit analysis. The fundamental principles of this procedure have been brought out by Bunnell and others (3), and need not be elaborated herein.

INDICATIONS FOR OPPONENS TRANSPLANT

The obvious indication for opponens transplant is lack of ability successfully to use the thumb, because of loss of its active opposition and abduction. Some individuals with relatively poor abduction and opposition of the thumb can still use their hand gainfully and do not desire reconstructive surgery. Others, with a similarly functioning thumb, feel handicapped by it in their particular type of work and therefore are in need of reconstruction. It is, then, a problem demanding not only an objective examination of the affected hand but concomitant consideration of the type of work which the patient must do with his hands.

In general, it can be stated that loss of ability to abduct the thumb to a distance of at least 1 inch (2.5 cm.) from the palm, with the tip of the thumb over the distal end of the third metacarpal bone, constitutes a fairly serious disability. This is particularly true when there is, combined with this, a lack of ability to rotate the thumb and to bring it across the palm so as to touch the tip of the little finger.

Individuals with complete paralysis of all the intrinsic muscles of the hand, such as results from damage to both the median and ulnar nerves, are in nearly all instances in need of opponens transplant. Roughly, however, 65 per cent of patients with paralysis only of the median-innervated intrinsic muscles substitute adequately, although in varying degrees of completeness, for loss of the opponens pollicis and abductor pollicis brevis muscles by means of the flexor pollicis brevis in combination with the abductor pollicis longus (Fig. 1). The remaining 35 per cent will require such a transplant in most instances.

These statements are based on our experience and that of others (2) that, in contrast to the median-innervated long flexors, the opponens pollicis and abductor pollicis brevis show actual return of motor function in only a small percentage of cases. This is true whether the injury to the median nerve has been incomplete and not requiring suture, or whether satisfactory neurorraphy has been carried out. Most of the 84 cases concerned herein were thus derived from the 618 cases of injury to the median nerve, some isolated and some combined with lesions of the ulnar nerve, seen among 3,276 injuries to peripheral nerves treated and studied in this neurosurgical center. The remainder were those in which there had been direct damage to musculature in the thenar eminence.

PREREQUISITES FOR SUCCESSFUL OPPONENS TRANSPLANT

The prerequisites for successful opponens transplant are a relatively loose and supple hand, the thumb of which can be brought passively into abduction, rotation, and oppo-

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sition; a suitable motor power to utilize in transfer; and a hand in such condition that it will be functionally improved by this procedure.

In the hand in which the thumb can be brought passively into the desired position with ease, there exists little problem and the results of transplant are excellent. In wounds of the upper extremities of such severity as to cause injury to peripheral nerves, however, there may have developed varying degrees of stiffness and fixed deformity of the hand. Such deformities never should be allowed to develop, but if once developed, they must be overcome prior to opponens transplant. By far the most important individual in overcoming these deformities is the patient himself. He must be made to understand thoroughly that his own constant working with the hand will improve it faster and more completely than will any other factor. Periods of work in a gainful occupation are unsurpassed as a means of obtaining this end. Proper splinting with constant, gentle traction by an apparatus so designed as to pull the thumb into abduction and opposition is an adjunct, but only an adjunct, to this active use of the hand.

The demand for an adequate motor power necessitates a musculotendinous unit in the forearm with sufficient strength to bring about opposition, abduction, and rotation of the thumb when the transplant has been properly completed, without sacrifice of useful function in the remainder of the hand. When only the intrinsic muscles of the hand are involved in the paralysis, there are of course a number of flexor tendons available. In injuries to the median and ulnar nerves in the upper arm in which there has been paralysis of the long flexor muscles, the surgeon should wait, after neurorraphy, until reinnervation of these muscles has proceeded to such a point that they have strength adequate for useful function when transferred. Occasionally, in cases of extensive damage to soft tissues involving the flexor tendons, the extensor carpi ulnaris proves to be the only available tendon; when utilized, it functions satisfactorily as a transplant.

It has been pointed out that a third prerequisite for this operation is a hand in such condition that it would be functionally improved by an opposable thumb. Sensation must be present in the hand, particularly in the thumb, and in the index and long fingers. Furthermore, there must be sufficient power in the fingers themselves to make them of value, along with the thumb. In a few individuals, particularly those in whom all four fingers flex in a mass as a result of tendon damage or a previous tendon transfer to the flexors of the fingers, the thumb is probably better utilized in adduction, in which it can perform a pincers type of action against the radial aspect of the proximal phalanx of the index finger. It is, then, important to emphasize again the necessity of accurately ascertaining whether the over-all usefulness of the hand will be improved by the new action of the thumb.

Although the absolute prerequisites for this procedure have been enumerated, there are other features which are desirable. It is, of course, advantageous to have relatively normal subcutaneous tissue for the rerouting of the transplanted tendons. This necessitates, in certain instances, the preliminary covering of the volar surface of the wrist and forearm with transplanted full-thickness skin by means of abdominal flaps or tubed pedicles. Occasionally, the use of a pre-formed sheath, as has been suggested by Milgram and others, will tend to diminish the tendency for adherence of the transferred tendon to surrounding structures. We have employed this in only 2 cases, and thus our experience is too limited to allow an appraisal of its value in opponens transplant. It is also desirable to have a strong action in the flexor pollicis longus tendon and reinforcement of this, if weak, at the time of opponens transplant is usually of value.

CHOICE OF OPERATIVE PROCEDURES

There are two main types of operative procedures which have been employed in this group of cases. One is the Bunnell type of opponens transfer; the second is the Thompson type. The Bunnell procedure (1) involves the use of a motor tendon, rerouted on the proximal side of the transverse carpal ligament and so transferred and attached to the thumb that the line of pull on the thumb is directed toward the pisiform bone. A pulley in the region of

the pisiform bone is usually employed. In the Thompson procedure, a sublimis tendon, preferably that to the ring finger, is severed within the flexor tendon sheath in the finger, rerouted on the distal side of the transverse carpal ligament, and inserted both proximal and distal to the metacarpophalangeal joint of the thumb. In this instance the palmar fascia, around which the tendon is rerouted, acts after a fashion as a pulley.

The Bunnell procedure was used in all instances possible. However, in not a few of our cases, there was found extensive scarring in the volar surface of the distal third of the forearm. In such individuals with marked forearm scarring and a normal palm, we felt that the Thompson procedure was advisable. By employing this, we were able to do all our transferring in normal tissue, and we thus avoided entering scarred areas.

Within the large group of transfers which follow the Bunnell principle, there are several useful variations. The basis of one group of these is the use of the extensor pollicis brevis as a means of prolonging the motor power employed. Such motor power can be supplied by means of the palmaris longus (Fig. 2), the flexor carpi ulnaris (Fig. 3), any one of the sublimis tendons, or even by the extensor carpi ulnaris. As will be noted, however, the extensor pollicis brevis is not always suitable for use.

A second group involves the use of a free tendon graft to prolong the motor power. Such a tendon graft can be inserted into the dorsal and proximal aspects of the proximal phalanx of the thumb and then rerouted subcutaneously toward the pisiform bone. A third subdivision within the Bunnell type is a procedure which we have come to consider very satisfactory; namely, the use of a sublimis tendon, preferably that to the ring finger, without the use of an intermediary graft. In this type of operation, the sublimis tendon is severed within the flexor tendon sheath of the finger very close to its point of insertion, and then is withdrawn well proximal to the transverse carpal ligament. It is then rerouted in the manner illustrated (Fig. 4), and is inserted at the proper tension into a drill hole on the dorsal aspect of the proximal phalanx of the thumb, in most instances. In a few cases, for reasons which will be discussed subsequently, it has been inserted into the distal end of the metacarpal bone.

TECHNICAL DETAILS OF OPERATIVE PROCEDURES

It is the purpose of this section to point out certain technical factors which seem to improve the results of opponens transplant. The principles common to all tendon-transfer procedures will not be repeated, but they are none the less of great importance. These include the use of a tourniquet, rigid adherence to aseptic precautions, and care in the rerouting of tendons. Proper, moderate tension on the complete transfer also must be obtained.

The placing of the incisions in the skin is an easily controlled factor which is of importance. It is always advisable, of course, to make incisions along skin tension lines, whenever possible. However, it has seemed in these cases even more desirable to so fashion these short incisions that they do not directly overlie tendons after rerouting, or particularly, the site of anastomosis of tendons. A few of the incisions employed in this group of cases are indicated in Figures 5 and 6.

In rerouting tendons from the pisiform bone across the palm up into the incision in the thumb, the finding of the proper plane for transfer is of great importance. This plane lies just superficial to the palmar fascia, and should be deep enough in respect to the skin itself so that the tendon does not become adherent to the overlying skin or so that pressure necrosis of the skin does not develop. This plane can be found by the passing of a long slim instrument, such as a uterine packing forceps, from the incision at the wrist, across the palm, and into the incision in the thumb.

When the extensor pollicis brevis is used as a means of prolonging the motor power, a few technical details are of some importance. First are accurate location and recognition of this tendon. In a few individuals the tendon is nonexistent. If it is present, it must be dissected out in such a manner that when it is pulled upon in the direction of the pisiform bone, it produces satisfactory opposition of the thumb. If it is dissected too far distally

across the metacarpophalangeal joint of the thumb, it will markedly flex this joint, which is undesirable. In a few instances, if the tendon is not dissected far enough distally, it will hyperextend this joint. Therefore, dissection must be carried out to just such a point that the desired rotation and opposition are obtained without either of the aforementioned undesirable actions. Occasionally, also, a slip connecting this tendon to the extensor pollicis longus must be severed so that it does not exert an extending action on the distal phalanx. In a few instances, despite severance of all connections to the long extensor tendon of the thumb, the extensor pollicis brevis continues to extend the distal phalanx. In such instances, it is probably best not to utilize this tendon, but to use a free tendon graft for prolongation of the motor power.

In most instances in which a sublimis tendon, usually that of the ring finger, has been rerouted and directly inserted into bone, the end of the tendon has been inserted into the proximal aspect of the proximal phalanx of the thumb. This has been carried out by the drilling of a small hole from well on the dorsal aspect of the phalanx down through both cortices, in such a way that the tendon inserted into it from the dorsal to the volar side imparts not only abduction to the thumb, but also rotation and opposition. The tendon is pulled down into the medullary cavity of the phalanx through the dorsal drill hole, and the pull-out wire technique of Bunnell is utilized to anchor it in place (Fig. 4).

A seemingly minor detail, but one of great importance when the aforementioned method is used, is the mobility of the metacarpophalangeal joint of the thumb. In a few cases this joint has been so mobile that it was impossible to insert the tendon into the proximal phalanx without the imparting of marked flexion at the metacarpophalangeal joint, in spite of a very proximal location of the drill hole. This possibility is explored by determination of whether or not traction on a suture passed through the drill hole in the phalanx exerts a satisfactory rotatory and opposing action on the thumb. If it does not, but instead causes marked flexion of the metacarpophalangeal joint, the tendon should not be inserted there, but must be inserted into the distal end of the metacarpal bone in a manner similar to that outlined for the phalanx. Despite any theoretic objection (1) to this site of insertion, the functional results have been excellent (Fig. 7).

In most procedures involving the Bunnell principle, some type of pulley must be utilized in the region of the pisiform bone. In instances in which the flexor carpi ulnaris is not utilized as a motor and in which it is functioning, the simplest and most satisfactory pulley is made by merely running the motor tendon around the flexor carpi ulnaris (Figs. 2 and 4). It is not advisable to mobilize the flexor carpi ulnaris, for this would allow it to bow somewhat radially. When the flexor carpi ulnaris is to be used as a motor or when it is nonfunctioning and thus would bow markedly to the radial side, the pulley can be constructed from part of this tendon as is shown in Figure 3. However, we have found that insertion of the proximal end of the segment left attached to the pisiform bone into a drill hole in the *very* distal end of the ulna provided a larger pulley and thus one with less tendency toward adherence to the tendon passing through it. Furthermore, the pulley constructed in this fashion does not swing as much to the radial side as do others. A third method of construction of a pulley is to use a short free tendon graft as a loop, both ends of which are inserted into two drill holes approximately 1 centimeter apart, placed in the distal end of the ulna. This is particularly valuable when the flexor carpi ulnaris already has been used for transfer into the extensor tendons of the fingers or when it is contemplated that such a transfer will be carried out. In any instance, anastomoses of tendons should be placed well away from whatever type of pulley is used, this usually being accomplished with ease. It is obvious that the presence of such a pulley near a tendon juncture would increase the possibility of adherence at that point. When the extensor carpi ulnaris is employed as a motor no pulley is necessary; the direction of pull of this tendon, after it has been rerouted, is toward the pisiform bone.

As noted earlier herein, we have on some occasions employed the Thompson procedure. We followed the technique originally described

Fig. 1. Satisfactory substitution in an individual with complete paralysis of the opponens pollicis-abductor muscle complex. The thenar muscle mass seen is the flexor pollicis brevis, innervated by the undamaged ulnar nerve.

by him, with the exception of the method of tendon insertion. In our cases, half of the sublimis tendon was inserted into a drill hole in the proximal end of the proximal phalanx of the thumb and the other half was inserted through a drill hole in the distal end of the metacarpal bone. These were fixed with the pull-out wire technique of Bunnell; or, on other occasions, they were pulled through the drill holes and anastomosed, one to the other, in the subcutaneous tissues of the ulnar side of the thumb.

The application of fixation at the conclusion of the operative procedure is of utmost importance. As the dressings are applied, the thumb must be worked into a position of opposition, abduction, and particularly rotation, with the use of numerous fluffed sponges and elastic bandage for accurate maintenance of this position. The metacarpophalangeal joint should be kept, if possible, in a very slightly flexed position. A molded posterior plaster-of-paris splint is used to reinforce this dressing, and straps are incorporated within it to provide a means of elevation of the hand for 72 to 96 hours postoperatively. When the entire dressing and splint have been applied, the

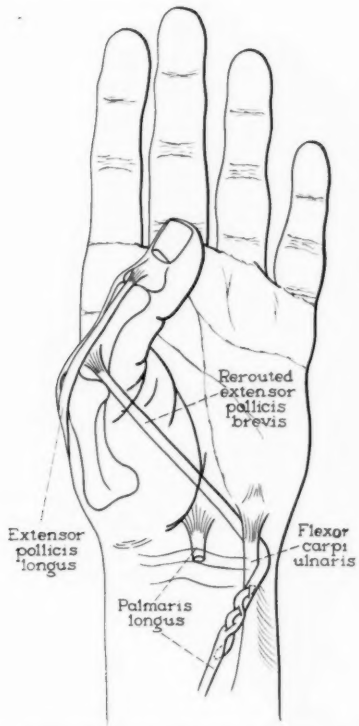


Fig. 2. Completed tendon transfer, in which the palmaris longus, rerouted around the flexor carpi ulnaris, is used and is prolonged with the extensor pollicis brevis.

thumb should be well out in abduction and rotation, and the wrist should be flexed to about 45 degrees.

POSTOPERATIVE CARE

The dressing is first changed at 21 days, at which time the pull-out wires are carefully withdrawn and the skin sutures are removed. The patient is then fitted with an adhesive and rubber-band type of splint, fashioned so as to pull the proximal phalanx of the thumb toward the pisiform bone (Fig. 8a and b). He is then carefully instructed *by the operating surgeon* as to precisely what tendon has been transferred and how he may learn to use this tendon for opposition of the thumb. He is urged to practice diligently with this transferred tendon, and for purposes of supervision in this he is referred to the Physical Therapy

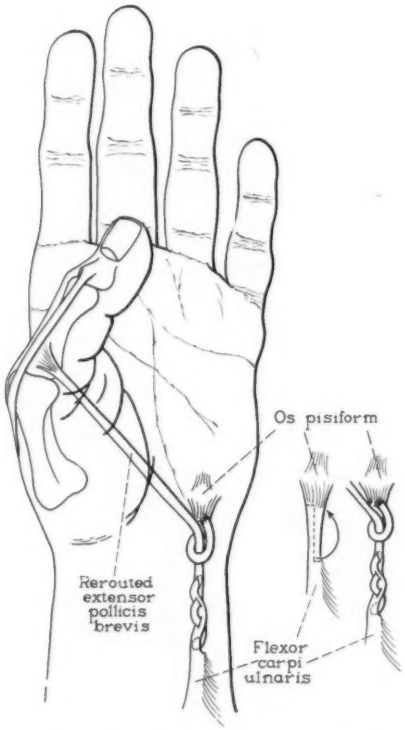


Fig. 3. Completed tendon transfer, involving use of the flexor carpi ulnaris prolonged with the extensor pollicis brevis. Insert shows method of construction of pulley in such cases.

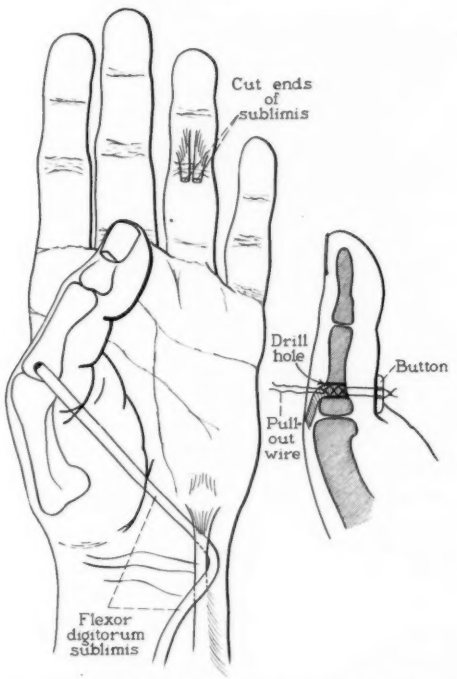


Fig. 4. Completed tendon transfer. The flexor digitorum sublimis of the ring finger is used, and is rerouted around the flexor carpi ulnaris and inserted into bone. Insert shows details of insertion of the tendon into the proximal phalanx of the thumb by means of a pull-out wire.

Department. After a period of about 5 days, gradual passive and active extension of the wrist is begun, and after another 5 days the patient usually has begun to use the transfer in acceptable fashion. He is then allowed to discard the splint and to begin active use of the hand. The patient's movements are watched until it is assured that he is using the transplanted tendon well. A period of about 6 weeks after operation usually is required in order that the patient may become completely automatic in the use of the rerouted tendon for opposition.

In a few instances the patients have been slow in learning the use of the transferred tendons. In such instances it is wise to prolong the period in which the elastic splint is worn, in order that the thumb may remain in a position of abduction, opposition, and rotation, rather than fall back against the hand.

SUPPLEMENTARY PROCEDURES

In instances in which an adduction deformity of the thumb cannot be overcome by the previously described nonoperative means, the adductor contracture present generally can be corrected by division of the adductor pollicis muscle at its point of insertion. Exposure is procured by the making of a short longitudinal dorsal incision between the first and second metacarpal bones. Care should be taken to keep this incision as far proximal as possible, thereby precluding undue tension on the skin suture line when the thumb is placed in opposition and abduction postoperatively. If there seems to be any contracture of the first dorsal interosseous muscle, it can be stripped

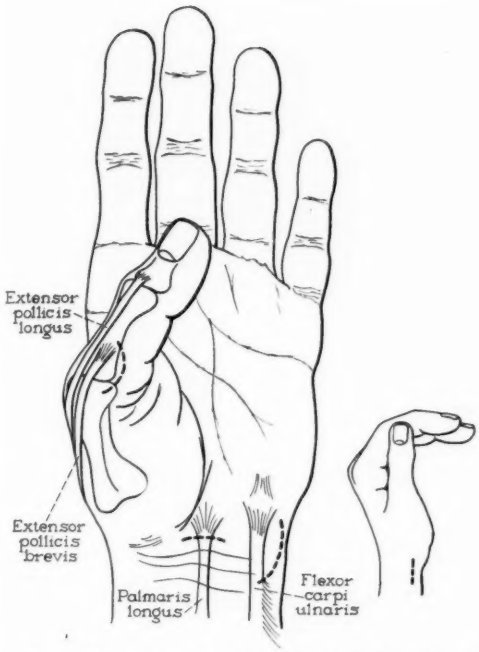


Fig. 5. Skin incisions (in dotted lines) for transfer of palmaris longus muscle as shown in Figure 2. In addition to those incisions shown, a small transverse incision over the palmaris longus muscle is made in the middle third of the forearm through which this tendon is withdrawn and rerouted toward the pisiform bone.

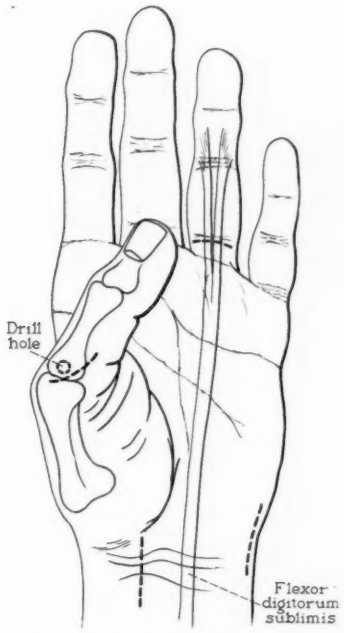


Fig. 6. Skin incisions (in dotted lines) for transfer of flexor digitorum sublimis of ring finger with direct insertion into the proximal phalanx as illustrated in Figure 4.

from the base of the first metacarpal bone through the same incision. These measures usually allow the thumb to be placed passively in the desired position. If sufficient release of the thumb still is not obtained, in certain cases some further benefit may be obtained by capsulotomy of the carpometacarpal joint. The results of this procedure, however, generally are less satisfactory than are those of severance of the adductor pollicis muscle.

Some residual paresis of the long flexors of the fingers occasionally occurs among these individuals. Most commonly the flexor digitorum profundus muscle to the index finger and the flexor pollicis longus are involved. If it is felt that this residual paresis is permanent, reinforcement of the function that is already present is indicated. The flexor digitorum profundus of the index finger usually can be joined to the remaining profundus mass; this should be done in such a position that with the long finger fully extended the index finger will be flexed to 45 degrees in all joints. Depending on the available tendons, the flexor pollicis longus muscle can be reinforced with the palmaris longus or with one of the sublimis tendons. Although the procedure is not an integral part of the opponens transplant, it will increase the strength of the thumb in opposition.

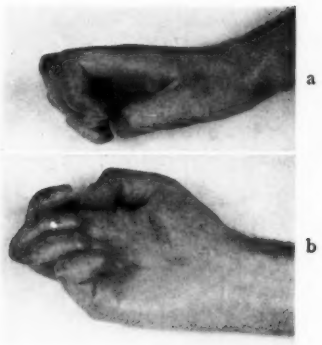
RESULTS

There are a total of 84 cases in this series, representing the results obtained by several different surgeons who used a variety of procedures. Information is available as to the methods employed in 75 cases. Of the 75 patients, 67 were observed or traced for sufficient time to allow adequate evaluation. The results were classified as "excellent," "satisfactory," and "unsatisfactory."

"Excellent" signifies the ability actively to abduct the thumb 2 inches (5 cm.) from the

a b

Fig. 7. Palmar, a, and lateral, b, views of excellent result after a Bunnell type of transfer, in which the flexor digitorum sublimis of the ring finger is utilized, with direct insertion in the distal end of the metacarpal bone, in a patient with complete paralysis of the intrinsic muscles.



a b

Fig. 9. Lateral, a, and palmar, b, typical preoperative appearance of a hand in which there is complete paralysis of the intrinsic muscles but not of the long flexor muscles.

palm; oppose it to the tip of the ring finger; and to rotate it so that the plane of the nail is within 20 degrees of the plane of the palm. These are essentially those movements possible in a normally functioning hand. If the thumb was deficient in the slightest degree in any of the above criteria, the result was *not* considered "excellent" but only "satisfactory."

In all cases in which movement of the thumb was rated "satisfactory," there was a decided improvement in function, and the patient was satisfied with his result.

In those cases in which there was no appreciable improvement over the preoperative condition, function was rated "unsatisfactory."

In Figure 9 is illustrated the typical preoperative function in all the hands concerned in the present study.

Among the 67 cases in which function was evaluated, it was classified as excellent in 30 (Figs. 10 and 11), and as satisfactory in 25 (Figs. 12 and 13). In 12 cases the result was judged to be failure. The data are summarized in Table I.

It is seen from examination of the data that every method is capable of giving a good result. In general, the degree of success was directly proportional to the completeness of fulfillment of the prerequisites for transplant without regard for the method employed. As an example, in hands with fixed deformities of sufficient severity to necessitate severance of the adductor pollicis muscle, there were no excellent results. However, although the results in these cases were given only a satisfactory rating, the functional result, considering the over-all condition of the hand, actually was an excellent one in each case, and it was felt that maximal improvement had been obtained.

The variety of methods utilized in this series resulted from the fact that many of the injuries were of such nature that the muscle

a b

Fig. 8. Palmar, a, and lateral, b, aspects of an elastic splint employed after removal of sutures on the twenty-first postoperative day.

a b

Fig. 10. a and b, Excellent result obtained after a Bunnell type of transfer, in which the flexor digitorum to the ring finger was utilized, with direct insertion into the proximal phalanx of the thumb, in a patient with complete paralysis of all the intrinsic muscles of the hand.

Fig. 11.

Fig. 12.

Fig. 11. Excellent result obtained after a Bunnell type of transfer, in which the palmaris longus muscle was utilized and was prolonged by the extensor pollicis brevis, in a patient with complete paralysis of all the intrinsic muscles of the hand.

Fig. 12. Satisfactory result after transfer of the palmaris longus muscle as in Figure 11, in a patient with complete paralysis of the intrinsic muscles of the hand.

used as motor power was the only one available. Therefore, the incidence of the methods does not accurately reflect the choice of procedures in cases in which the injuries were uncomplicated.

The question naturally arises as to the deficits resulting from transfer of the motor tendon. The rerouting of the palmaris longus muscle, of course, results in no loss of function. Similarly, there is essentially no disability when the flexor carpi ulnaris or extensor carpi ulnaris is used. The function of a flexor digitorum sublimis, when it is transferred is taken over by the flexor digitorum profundus in question to such an extent that its absence cannot be determined by clinical examination. In no instance has any patient felt that his finger was noticeably weakened by transfer of a flexor digitorum sublimis.

ANALYSIS OF FAILURES

In this series there were, as previously pointed out, 12 cases in which the result was classified as unsatisfactory. An analysis of these cases is enlightening as to pitfalls to be avoided.

In 2 instances the thumb was in good position 3 weeks postoperatively, but returned to an adducted position during the ensuing 2 to 3 weeks and never showed active opposition. In both of these cases the operative sites were re-explored; in the first instance the anastomosis between the palmaris longus and extensor pollicis brevis was found to have disrupted. The flexor digitorum sublimis to the fourth finger was then utilized as a motor; it was inserted into the proximal phalanx of the thumb, with an excellent result. In the second instance the short extensor had apparently disrupted from its insertion over the proximal phalanx, probably because of excessive dissection. The flexor digitorum sublimis to the third finger (that to the fourth having been utilized in the previous procedure), was then used; it was inserted into a drill hole, with resulting excellent function. From the experience reflected in these 2 cases it should be concluded that re-exploration is indicated in cases in which the function of opposition and abduction is not manifested postoperatively.

a b

Fig. 13. Palmar, a, and lateral, b, aspects of a satisfactory result after a Thompson procedure. More opposition was possible than is shown here.

TABLE I.—RESULTS OF OPPONENS TRANSPLANT IN 75 CASES, ANALYZED ACCORDING TO TYPE OF PROCEDURE EMPLOYED*

Procedures, types	Results in evaluated cases			Cases not evaluated
	Excellent	Satisfactory	Unsatisfactory	
Palmaris longus	8	9	3	3
a. Prolonged with extensor pollicis brevis	8	7	3	3
b. Prolonged with free graft	0	2	0	0
Flexor carpi ulnaris	5	4	3	2
a. Prolonged with extensor pollicis brevis	4	4	2	2
b. Prolonged with free graft	1	0	1	0
Flexor digitorum sublimis, fourth finger	3	1	2	0
a. Prolonged with extensor pollicis brevis	3	0	1	0
b. Prolonged with free graft	0	1	1	0
Extensor carpi ulnaris	4	1	2	0
a. Prolonged with extensor pollicis brevis	4	0	2	0
b. Prolonged with free graft	0	1	0	0
Flexor digitorum sublimis with direct insertion	6	8	1	3
a. Sublimis of ring finger	5	6	1	3
b. Others	1	2	0	1
Thompson method	4	2	1	0
a. Sublimis of ring finger	4	1	1	0
b. Sublimis of ring finger	0	1	0	0
Total	30	25	12	8†

*Except for the group entitled "Thompson method," the Bunnell type of procedure was employed and the designated tendon was used as a motor source.

†In 9 additional cases no information was available as to the details of the procedure employed or the results obtained.

In 3 instances of failure, the opponens transplant was but one part of a multiple-tendon transfer procedure. This resulted in compromise in the securing of correct tension and ideal position, with ultimate failure. When other tendon transplant operations about the wrist are performed, the opponens procedure usually will profit by being postponed to a later date. This, in addition, simplifies the problem of re-education for the patient.

In 2 cases the tension on the completed anastomosis was extremely slight, which may well explain the failure which occurred. Fixed deformities of parts of the hand other than the thumb were present in 2 cases, and were of such severity that they could not be overcome. Operation for these individuals was ill-advised, and the resulting failure could be anticipated. In another instance, because of an unfortunate oversight, the motor utilized was a paralyzed muscle. In 2 cases the causes of failure were undetermined because the patients had been dismissed from the hospital and thus were not available for evaluation.

This analysis of the failures serves well to emphasize the prerequisites, since in many of the aforementioned instances they were not present, and failure followed. We feel that in future cases there should be no instances of failure.

COMMENT AND CONCLUSIONS

A series of cases has been presented in which a variety of types of opponens transplant was carried out. The indications and prerequisites for this procedure have been discussed, and the technical details of importance have been related. An analysis of the series has been presented in an attempt to judge the end results. The failures have been discussed with a view to prevention of such poor results in future cases.

The over-all study of this group of cases allows the formation of some conclusions as to the methods of choice to be employed. In the usual case, it is probably preferable to use the Bunnell type of operation, since the Thompson procedure, although satisfactory, fails to give quite as much abduction as does the former type. In cases in which there is marked scarring about the volar surface of the wrist, the Thompson procedure is preferable in order that the operation may be carried out in normal tissue.

When the Bunnell method is employed, it is probable that a good result can be obtained from the use of any source of motor power. In instances in which all possible sources of motor power are available in good strength, including a rather strong palmaris longus muscle, and cases in which the extensor pollicis brevis on surgical exploration is found to be sturdy and to give the desired action on the thumb, the use of these in the manner described (Fig. 2) is very satisfactory. If the palmaris longus is thin or weak, however, or if the short extensor of the thumb is attenuated or exerts a poor

action on the thumb, it is probably wise not to employ this method, but to use instead the flexor digitorum sublimis tendon to the ring finger severed within the digital sheath, with direct insertion of it into the thumb in the manner described (Fig. 4). Furthermore, if there is some adduction deformity of the thumb and a strong motor source is desired, such use of the flexor digitorum sublimis to the fourth finger is of even greater advantage.

In point of fact, the use of this method has certain definite advantages over all others. It provides very strong motor power, with excellent excursion. There is no anastomotic site to become adherent to surrounding structures. The insertion of the tendon into bone is so durable as to render disruption virtually impossible. At present, it would be our method of choice.

If these tendons are not available, however, a good result can be procured by carrying out an accurate procedure in which any of the methods discussed are employed. The important considerations are attention to the prerequisites for a good result, and care as to the technical details of the operative procedure.

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TREATMENT OF PERSISTENT COLON BACILLUS INFECTIONS OF THE URINARY TRACT BY SULFASUXIDINE AND STREPTOMYCIN

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MODERN drug and antibiotic therapy has enabled us to eradicate a large percentage of the nonsurgical infections of the urinary tract in a manner which would have seemed almost miraculous a decade ago. There are, however, a number of patients, both male and female, who respond favorably to treatment for a short time but who suffer recurrence of infection shortly after therapy is discontinued; still other patients do not achieve permanent urine sterilization by any previously employed combination of medical or instrumental treatment.

It is well to initiate this discussion by emphasizing the fact that the efficiency of modern urinary antiseptics should in no way moderate the absolute necessity for a thorough urological examination in each patient suffering from a urinary tract infection. The search for, as well as the eradication of, any extraurinary focus of infection remains as important today as it was heretofore. The correction of any lesion which causes obstruction to the free outflow of urine is of paramount importance before medical management can be permanently successful.

Our experience parallels that of most other observers in that we have found a predominance of the colon-typhoid, or coliform, group of organisms as the main cause of urinary tract infection. In most individuals in whom there is no associated obstructive uropathy the urinary infection can be eradicated by the removal of systemic foci of infection and the administration of the proper urinary antiseptics. The ingestion of mandelic acid or sulfa derivatives, or the alternate use of these drugs, has been effective in a large percentage of our patients when the colon bacillus has been the principal infecting agent. Where coccal organisms are also present in the urine, penicillin is indicated in conjunction with sulfa or mandelic acid compounds. At times the older urinary antiseptics, such as hexamethylenamine in its various forms, may prove effective in sterilizing the urine when our modern drugs have failed.

Herrold has recently suggested methods for *in vitro* tests of susceptibility to penicillin and streptomycin of the bacteria found in nonspecific infections of the urinary tract. "Tests of susceptibility by using exudates or urines enable a prompt grading and, in addition, where mixed infections occur, the relative susceptibility of the various organisms can be determined."

Wider clinical application of these principles may enable us to determine more quickly which medication is most applicable for the patient at hand. Despite our increased success in the treatment of colon bacillus infections of the urinary tract with the newer antiseptics and antibiotics, we continue to encounter individuals in whom we have eliminated all extraurinary foci and in whom we have repeatedly demonstrated that there is no obstructive uropathy, but where we have been unable to clear the urine permanently of the infecting organisms by varied medication.

The question naturally arises: Why do these individuals continue to have recurrences? Is it because they are infected with an unusually virulent strain of bacteria or do they continue to have a systemic focus of infection which reinfects the urinary tract?

Kauffman of Copenhagen has shown that certain strains of colon bacilli are recognized

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as important etiological agents in infections of the urinary and bile tracts and particularly in producing appendicitis. While we have all agreed that the transfer of organisms from the large bowel to the urinary tract can, and does, frequently occur, clinical proof of this is often difficult or impossible. Our interest in further attempting to limit the colon bacillus content of the large bowel by sulfasuxidine was stimulated by the report of Everett, Scott, and Steptoe who described the successful use of this drug in the treatment of acute pyelitis of pregnancy due to the colon bacillus in pure or mixed culture.

Our recent associate, Dr. Robert McAllister, began the treatment of a group of patients with resistant urinary tract infections by giving sulfathaladine, and later sulfasuxidine, as the sole medication. From 8 to 10 grams of the drug were given daily for the first 2 weeks and then 4 to 5 grams daily for an indeterminate period of from 8 weeks to 10 months. In general this selected group of patients responded favorably to this treatment. The urinary symptoms were reduced, constipation was often completely relieved and the pyuria was diminished. These patients experienced enough improvement to be willing to continue the therapy. Despite the prolonged ingestion of sulfasuxidine they were remarkably free of toxic symptoms. One woman complained of dizziness and anorexia and these symptoms subsided promptly with discontinuance of the drug. Patients may be sensitive to sulfasuxidine but Bargen found the toxic reactions of sufficient severity to indicate discontinuance of the drug in only 1 per cent of 2000 patients. Roth reported an occasional skin eruption, or febrile reaction, in patients sensitive to sulfathiazole. Hematuria and crystalluria in one patient were reported by Clay and Pickrell. In 1943 Johnson reported a fatal instance of agranulocytosis apparently due to sulfasuxidine. None of these complications developed in our patients. Despite the clinical improvement sustained during this therapy, the colon bacilli persisted in the urine or recurred shortly after discontinuing treatment.

Sulfasuxidine is the trade name for succinylsulfathiazole. About 5 per cent of the drug is said to be excreted in the urine as sulfathiazole. Roth and his associates reported a blood level of free sulfathiazole rarely above 1.5 milligrams per cent in patients taking .25 gram per kilogram weight in six divided doses every 24 hours. Extensive studies have proved that both sulfasuxidine and sulfathiazole are sparingly absorbed from the bowel and have their action limited largely to the gastrointestinal tract. Roth has stated: "the amount of drug required to alter the intestinal flora will be determined by the content of the bowel, its mucosal surface area, and the rate at which the drug passes over the surface rather than by the weight of the patient. The coliform bacilli in the feces is reduced to less than 1000 organisms per gram of wet stool when 3.0 grams of sulfasuxidine is given by mouth every 4 hours to adults in the following times: (1) 37 per cent in 3 days of therapy; (2) 80 per cent within 5 days; and (3) 94 per cent within seven days." The stools become semifluid, smaller in bulk, relatively odorless and there may be three to four movements a day. A voluminous literature with many detailed case reports verify the value of this drug in the preparation of the bowel for extensive surgical procedures.

During the course of the above study a few grams of streptomycin became available to us for experimental purposes. Because of the extreme resistance of a colon bacillus infection in the only remaining kidney of a man, 60 years of age, who had previously received all manner of modern treatment and who had been on sulfasuxidine with slight improvement for 3 months, a total of 5 grams of streptomycin were administered to him over a period of 6 days. The urine rapidly cleared to complete in 3 days, with negative cultures after the fifth day. This patient was continued on 4 grams of sulfasuxidine daily for 4 months after leaving the hospital. It is now 16 months since the urine has shown pus or bacteria. The apparent complete cure of this most resistant infection by combined sulfasuxidine and streptomycin administration has prompted us to use this combination in a series of 23 patients. All of these patients had been under observation for from 3 months to 20 years without an effective or lasting eradication of the colon bacillus from the urine. The results obtained

have been so uniformly successful, and so much more noteworthy than when streptomycin alone was employed, that we feel this combination offers the possibility of an effective method of cure in a greater percentage of these resistant cases than has been obtained by other methods of medication heretofore employed.

In attempting to explain the reason for urine sterilization in these patients, in whom all previous methods had failed, the question naturally arises as to whether or not this combined medication has succeeded because it has lessened the colon bacillus transfer from the bowel to the urinary tract and thus permitted the natural immunity of the individual to complete the eradication of the infection.

Reports, which are daily becoming more frequent, of the results one may expect to obtain by the administration of streptomycin for colon bacillus infection of the urinary tract suggest a favorable response in 45 per cent to 60 per cent. The committee on chemotherapeutics (Keefer and associates) reported a 52 per cent recovery in 154 patients with Escherichia coli infection of the urine: 25 per cent improved and 21 per cent not affected. Of the patients that improved 19 per cent relapsed after treatment was stopped. Nearly all the relapses occurred in one week. Findlay reported the failure of streptomycin in 5 of 6 cases of Bacillus coli infection of the urinary tract. He explained the failure as being due to the rapid development of extreme resistance to the antibiotic.

The favorable response in our patients has been approximately 85 per cent. That the streptomycin alone has not been the conclusive factor seems demonstrated by the fact that those of our patients who could not tolerate the continued ingestion of sulfasuxidine had a relapse of urinary infection. This relapse occurred in 2 of our patients.

CASE REPORTS

Mrs. J. K., age 60 years, gave a history of intermittent attacks of chills, fever and pyuria for a period of 33 years. Urine cultures showed a heavy growth of Escherichia coli. The pyelographic studies were negative for obstructive uropathy. All types of urinary antiseptics had been administered. On a few occasions the urine cleared of pus but negative cultures were never reported. On May 20, 1946 this patient entered Wesley Memorial Hospital. Five million units of streptomycin were administered. Cultures of the urine were reported as negative on May 26. Two days before leaving the hospital the patient developed an intolerance for the sulfasuxidine and refused to take further dosage of the drug. Subsequent cultures taken at the office were reported as follows: June 12, 1946, negative after 48 hours, July 23, 1946, negative after 48 hours, August 24, 1946, negative after 48 hours, December 18, 1946, Bacillus coli; January 13, 1947, Bacillus coli; May 15, 1947, Bacillus coli.

Mrs. O. W., age 48 years, gave a history of "chronic cystitis." All manner of urinary antiseptics had been tried but cultures were always positive for colon bacilli. This patient entered Wesley Memorial Hospital on May 23, 1946. The urine showed Escherichia coli; 5 million units of streptomycin were administered. Cultures of the urine were negative on June 3 and 8. The sulfasuxidine had to be discontinued because her referring doctor was sure it interfered with the patient's ulcer management and aggravated the ulcer pain. Subsequent cultures at the office were reported as follows: July 8, 1946, Bacillus coli; August 26, 1946, negative; October 18, 1946, negative; November 6, 1946, Bacillus coli; November 18, 1946, Bacillus coli; May 12, 1947, Bacillus coli.

We were unable to obtain negative cultures at any time in 2 of our 23 patients.

Mrs. L. W., age 65 years, gave a history of a right nephrectomy in 1932 for a calculous pyonephrosis. In December 1944, a left nephrostomy with pyeloplasty was performed for a pyohydronephrosis. There was good visualization of kidney and emptying time of the pelvis and bladder. Sulfasuxidine (4 grams daily) was administered for 8 months before the first 5 million units of streptomycin were given. The urine became clear but remained positive for Escherichia coli. A second course of streptomycin (12 million units) was prescribed but the cultures remained positive. Following the streptomycin the patient developed dizziness and inco-ordination. Nine months have passed since the streptomycin was given. The dizziness had completely disappeared. A culture on May 17, 1947 was positive for Bacillus coli. Urine showed 10 to 20 pus cells per high-power field.

The second case that failed to show negative cultures at any time on combined sulfasuxidine and streptomycin therapy was that of Mrs. H. G., age 34 years.

Retrograde and intravenous pyelograms showed a hypoplasia of the right kidney. We believe the function of this kidney was too poor to concentrate the streptomycin in sufficient unitage to inhibit bacterial growth. A nephrectomy is probably indicated.

TABLE I.—SUMMARY OF 23 CASES

Case No.	Culture	4.0 to 8.0 Sulfasuxidine before hospitalization for Streptococcus	Grams of streptomycin	Sulfasuxidine after leaving hospital	Date of admission to Wesley Memorial Hospital	Date of beginning streptomycin therapy	Case No.	Date of report of first neg. culture	Subsequent cultures	Age of patient Sex	Previous surgery (G4)	Duration of recurrent attack	Comment
[1] L. W	Esch. coli	+	17	4.0 daily	2–18–1946 9–27–1946	2–19–1946 9–27–1946	1	Always positive	Positive Esch. coli	65 F.	1932—Calculus pyonephrosis 1944 Left nephrectomy	18 yrs.	Recurrence May, 1947
[2] K. K.	Esch. coli	+	5	None	5–20–1946	5–20–1946	2	5–26–1946	Positive 12–18–1946	60 F.	None	33 yrs.	Mild recurrence April 1947
[3] E. D.	Esch. coli	+	5	4.0 daily	4– 9–1946	4–20–1946	3	4–30–1946	Negative	44 F.	None	1–2 yrs.	Neg. May 1947
[4] P. McG.	Esch. coli	+	5	4.0 daily	4–25–1946	5– 1–1946	4	5– 5–1946	Negative	55 F.	None	10 yrs.	Neg. May 1947
[5] E. H.	Esch. coli	+	5	4.0 daily	5– 8–1946	5–14–1946	5	5–17–1946	Negative	50 F.	None	4 yrs.	Neg. May 1947
[6] W. C. O.	Esch. coli	+	5	4.0 daily	5–18–1946	5–20–1946	6	5–25–1946	Negative	61 F.	None	1 yr.	Neg. May 1947
[7] O. W.	Esch. coli	+	5	None	5–23–1946	5–31–1946	7	6– 3–1946	Positive 7– 8–1946	48 F.	1945 Caruncle	2–3 yrs.	Neg. Apr. 1947
[8] R. T. J.	Esch. coli	+	5	4.0 daily	5–24–1946	5–24–1946	8	5–29–1946	Negative	52 M.	1942 Left nephrolithiasis	15 yrs.	Neg. Apr. 1947
[9] G. H.	Esch. coli	+	5	4.0 daily	8–12–1946	9– 6–1946	9	9– 6–1946	Negative	68 F.	None	1 yr.	Neg. Apr. 1947
[10] M. C.	Esch. coli	+	5	4.0 daily	9– 6–1946	9– 6–1946	10	9– 9–1946	Negative	65 F.	None	10 yrs.	Neg. Apr. 1947
[11] A. N.	B. coli	+	5	4.0 daily	9–20–1946	9–20–1946	11	9–23–1946	Negative	58 F.	None	1 yr.	No check up
[12] R. T.	Esch. coli	+	5	4.0 daily	9–17–1946	9–17–1946	12	9–20–1946	Negative	45 M.	None	6 mos.	No check up
[13] B. S.	Esch. coli	+	5	4.0 daily	9–26–1946	9–26–1946	13	9–28–1946	Negative	50 M.	1944 Two T.U.R. 1945 T.U.R.	3 yrs.	Neg. May 1947
[14] M. P.	Esch. coli	+	5	4.0 daily	9–30–1946	10– 5–1946	14	10–10–1946	Negative	41 M.	None	1 yr.	Neg. May 1947
[15] F. E. G.	B. coli	+	5	3.0 daily	10–18–1946	10–18–1946	15	10–22–1946	Negative	66 M.	1941 T.U.R. 1944 T.U.R. 1945 T.U.R.	6 yrs.	Neg. May 1947
[16] M. R.	B. coli	+	5	None	11– 3–1946	11– 3–1946	16	11– 9–1946	Negative	62 M.	1946 Coagulation of Ca bladder	1½ yrs.	Neg. May 1947
[17] B. P.	Esch. coli	+	5	4.0 daily	11– 2–1946	11– 4–1946	17	11–11–1946	Negative	55 M.	1946 Coagulation of polyps of vesical neck	29 yrs.	Neg. May 1947
[18] P. H.	Aerobacter aerogenes	+	5	4.0 daily	11–20–1946	11–21–1946	18	11–26–1946	Negative	56 M.	1942 carcinoma of bladder, coagulated. 1943 Bladder, Transplantation of ureter	5 yrs.	Neg. May 1947
[19] L. K.	Esch. coli	+	5	3.0 daily	11– 5–1946	11–14–1946	19	11–27–1946	Negative	54 F.	None	2 yrs.	Neg. Apr. 1947 Neg. May 1947
[20] T. T.	Esch. coli	+	5	4.0 daily	2– 2–1946	2– 3–1946	20	2– 8–1946	Negative	60 M.	1944 Prostatectomy left ureterolithiasis 1945 Left nephrectomy	3–5 yrs.	Pos. May 1947
[21] H. G.	B. coli	+	5	4.0 daily	11–18–1946	11–18–1946	21	Positive Escherichia	Esch. coli 11–23–1946	34 F.	None	28 yrs.	Hypoplastic right kidney
[22] R. K.	B. coli	+	5	4.0 daily	1–22–1947	1–22–1947	22	1–27–1947	Negative	73 M.	1940 T.U.R. 1946 T.U.R.	7 yrs.	Neg. May 1947
[23] A. G.	B. coli	+	5	4.0 daily	1–18–1947	1–21–1947	23	1–25–1947	Negative	23 F.	None	1 yr.	Neg. May 1947

T.U.R., transureteral resection.

To the present time 19 of our 23 patients have sterile urine. In none of these cases was more than 5 grams of streptomycin administered. Sulfasuxidine was given before, during, and following the administration of the antibiotic.

The following brief case histories illustrate the type of patient so treated.

R. J., age 52 years, white male, gave a history of pyuria of 15 years' duration. In 1942 a left nephrolithotomy was performed. Urine cultures have been persistently positive for Bacillus coli in spite of the liberal administration of penicillin, sulfonamides, mandelic acid, urotropin and mandelamine. Retrograde pyelograms showed a left middle hydrocalyx. A negative urine culture was obtained after 3 million units of streptomycin had been given. A total of 5 million units were administered. Urine cultures have been taken at 2 to 4 week intervals, and all have been negative for growth. The patient left the hospital on May 24, 1946. He continued to take 4 grams of sulfasuxidine daily without toxic effects for 5 months. April 18, 1947, urine cultures were negative.

B. S., age 50 years. This patient had two transurethral resections of the vesical neck in 1944 and a third in 1945. Intravenous pyelograms showed normal outlines. Urine cultures were positive for Bacillus coli. After a preliminary course of sulfasuxidine, this patient entered Wesley on September 26, 1946, for a course of 5 grams of streptomycin. Urine cultures were sterile on the 28th and 29th. All subsequent cultures have been negative. About 2 months ago the patient discontinued the sulfasuxidine of his own volition because he thought "it was becoming toxic to him." The last culture on May 15, 1947 was negative. The urine is clear, free of pus and the patient is well in every respect.

F. G., age 66 years. This patient, like the one just reported, had had three transurethral prostatic resections; the first in 1941, second in 1944, and, third in 1945. Symptoms of nocturia, frequency and burning persisted because of a chronic cystitis due to Bacillus coli infection. The severity of the symptoms was modified by the use of sulfasuxidine. On October 18, 1946, the patient entered Wesley Memorial Hospital. A negative urine culture was obtained after the administration of 4 grams of streptomycin. The urine is negative to the present time. The patient has taken 3 grams of sulfasuxidine daily for 7 months.

P. H., age 56 years. Five years ago a papillary carcinoma of the bladder was coagulated transurethrally. In February of 1943 the left ureter was transplanted into the bladder because of a stricture of the orifice. The urine has been cloudy with pus. Urine cultures showed a heavy growth of Aerobacter aerogenes. On November 21, 1946 the patient entered Wesley Memorial Hospital. A cystoscopic study showed a slight enlargement of the median and left lateral lobes of the prostate. A retrograde pyeloureterogram showed a grade II left hydronephrosis. Five million units of streptomycin were given. Urine cultures were reported as negative on November 26. The pus count was 2 to 4 cells per high-power field as compared with numerous cells on admission. Subsequent cultures have been negative. This patient continued to take 4 grams of sulfasuxidine daily for 6 months. Cultures on June 10, 1947 were negative.

Fifteen female and 8 male patients varying in age from 73 to 23 years have been studied in detail. Each of these patients had an unusually resistant urinary infection, 22 with positive urine cultures for Escherichia coli and one with Aerobacter aerogenes. Obstructive lesions in the urinary tract were ruled out in each patient by complete investigation. The duration of recurrent urinary infection ranged from 33 years to 1 year. The average time for the entire group was 8 years. Ten of these 23 patients had had surgical operations upon the urinary tract.

It is now 17 months since the first patient was placed upon the combined therapy of sulfasuxidine and streptomycin (Case 1). His urine has remained negative to culture and free of pus for this time. Prior to this treatment his urine had been constantly infected for a period of 5 years. Two patients have had sterile urine for 14 months; 2 for 12 months; 2 for 9 months; 6 for 8 months; 1 for 7 months; 4 for 6 months and 2 for 4 months.

CONCLUSION

We are of the opinion that this series of patients, although small in number, suggests an unusual efficacy in the combined administration of sulfasuxidine and streptomycin in otherwise resistant bacillary infections of the urinary tract.

Of 23 patients so treated 19 have maintained a completely favorable response for periods sufficiently prolonged to suggest the probability of permanent cure. As previously described in detail, these patients received sulfasuxidine for varying periods before, during, and after the administration of 5 to 17 grams of streptomycin.

Sulfasuxidine or streptomycin given alone has not had the favorable effect observed in the combined therapy. Success in the 19 patients with long-standing resistant infection

seemed dependent upon the patients' ability to continue the ingestion of sulfasuxidine. Fortunately the toxicity of sulfasuxidine is low and the drug can be given in large doses for long periods of time.

Toxic symptoms, if they occur, subside rapidly when the drug is discontinued.

This study is reported in detail in the hope that it will encourage a more widespread trial of this, or some similar, combined therapy in the treatment of otherwise resistant urinary infections of bacillary origin.

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THE RADICAL TREATMENT OF BRAIN ABSCESS

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BRAIN abscess is generally considered to be one of the most serious pathological conditions of the central nervous system, the treatment of which is difficult and the prognosis doubtful. It seems, however, that such a pessimistic view is unfounded and its existence best explained by the consequences of the mistakes physicians often commit in not distinguishing between the two different stages of one and the same disease, e.g., between the purulent encephalitis and the abscess proper. Consequently, operative treatment, which is indicated for an abscess, is applied when the suppurative process has still not been localized, that is, when there is no indication for surgical intervention. It is difficult, indeed, to treat an abscess before it has formed.

Success in the treatment of cerebral abscess depends principally upon the moment surgical intervention is applied. The excellent and up to now unparalleled results obtained by Macewen, who from his 19 patients suffering from cerebral and cerebellar abscesses, lost only 1, were chiefly due to the fact that he never used drainage in an acute stage of the disease but waited for proper encapsulation of the abscess.[1] He was, no doubt, entitled to say that "an uncomplicated brain abscess may be regarded as the most hopeful of all cerebral affections."

According to Adson and Craig: "it took us many years to learn that hasty emergency operations were futile and were accompanied by high mortality. This, undoubtedly, was due to the insistence of colleagues that we do something as soon as a diagnosis of cerebral abscess has been made."

We must then define the term "abscess," in order to find a reason for the somewhat unsuccessful results obtained in the treatment of cerebral abscesses. Experience shows that these are due not so much to mistakes in diagnosis or localization of the lesion as to the improper time chosen for operation. "No experienced surgeon would consider incising and draining an abscess in any other area of the body before encapsulation was completed" (18). Why, then, do so many surgeons behave differently in a case of cerebral abscess?

An abscess is, according to Lecène "a collection of pus in a new formed cavity, distinctly limited from the surrounding tissue and which represents the end-result of an acute inflammatory process." The accent lies here on the statement that the abscess is the "end-result of an acute inflammatory process" and that it is distinctly separated from the surrounding tissue.

"The reaction of the brain to focal purulent infection resembles the reaction of the other organs of the body to such a process in that there is rapidly formed a mesoblastic barrier about the bacterial focus. That is, of course, assuming the infection can be limited at all" (41). An abscess is the result of a protective process which is advantageous to the body and testifies to its resistance to the pathogenic organisms. If, on the other hand, the virulence of the organisms is too great or the resistance of the body too weak, no abscess will develop and the local inflammation of the brain will change into an encephalitis spreading over one or even both cerebral hemispheres.

The first fibroblasts, that is, the first signs of a capsule, appear around the liquefying focus of inflammation at the end of the first week, the capsule becoming mature and offering firm elastic resistance to the exploring brain needle only at the end of the second or even the third week (17, 21, 41). The development of a firm capsule requires a somewhat longer time in the case of an abscess of the

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[1]According to Fay, Ambroise Paré reported in 1568 a series of cases of abscess of the brain with a remarkably low operative mortality. This was mainly due to the fact that he awaited localization and encapsulation of the abscess before operating. He first trephined the skull over the lesion and 3 days later incised the dura mater allowing the brain to bulge forth. For drainage he used lead cannulas.

brain than in similar lesions located elsewhere in the body, probably because the brain contains less connective tissue and it is connective tissue which is the decisive element in any encapsulation. Actually, Huguenin missed the capsule in an abscess of 32 days' duration, and in another of 53 days' duration, the capsule was still very thin. He found a thick, elastic capsule only in a case of a brain abscess which had lasted for 83 days. Bergmann (6) states that Meyer examined the formation of the capsule in 21 cases of posttraumatic cerebral abscesses and came to the conclusion that the first signs of encapsulation appear 19, 20, and 25 days after the infection, the capsule becoming firm only in the sixth week of the disease. According to McKenzie, a cerebral abscess is well encapsulated 4 to 5 weeks after the infection. Grant found that in the first 2 weeks of the disease only 3 out of 13 abscesses were encapsulated; between the third and fourth week 10 out of 18 already had a well developed capsule; and after 6 weeks, all abscesses were definitely and distinctly walled off. Groff asserts that the resistance of the capsule to the exploring needle is well marked at the end of the third week after infection, and Kahn states that he observed a patient in whom an abscess of 10 days' duration was already well encapsulated.

It is obvious, therefore, that the time necessary for the development of a capsule varies in each case, this fact being most probably due to a number of circumstances, such as, individual differences in the virulence of the organisms, method of invasion, degree of resistance of the body, etc.

However, it may be that one should not expect a cerebral abscess to be well encapsulated before the end of the third week after the infection and that before that time there is little hope for surgical intervention to end successfully. According to Grant who studied in detail the relationship between the success of the treatment and the duration of the disease, the mortality in 30 cases of encapsulated abscesses was 33.3 per cent, while in the 19 cases of unencapsulated abscesses it reached 100 per cent. The best operative results were obtained when the patients were treated 4 to 6 weeks after the infection. If a patient dies before the abscess is properly encapsulated, that is, before the proper time for operation is reached, the reason lies not in the postponement of surgical intervention, which at that time could only have been harmful, but in the absence of sufficient resistance of the body to the infection. The rupture of a well encapsulated abscess rarely occurs; more often the patients die because of an operation performed too early than because of surgical intervention applied too late. Out of 49 patients of Grant, only 2 died because operation was delayed too long, but 14 died because it was performed too soon.

There is now indeed no divergence of opinion as to the fact that operation for a cerebral abscess before capsule formation has taken place is nearly always fatal, yet the choice of the preferable procedure is still a much debated question. The treatment indicated is always surgical because although there are undoubtedly cases of brain abscess which come to self-healing, such an occurrence is very rare and the disease, not properly treated, ends sooner or later in death of the patient.

Without entering here any details of the history of the surgical procedures which have been and are still carried out in the treatment of cerebral abscess it is sufficient to say that the following are the most frequently used: (1) single or repeated tappings of the abscess with emptying of its contents and with or without the introduction of penicillin into the abscess cavity; (2) drainage of the abscess; (3) extirpation of the abscess, either intact or after evacuation of its contents. This last method of treatment seems to us to be the most rational but it has up to now been used by the majority of surgeons rather reluctantly. It is difficult to perceive the advantage of tapping or draining an encapsulated abscess over its removal *in toto*. On the contrary, it seems that there are many reasons why the last procedure should be the method of choice. It is as safe for the patient as the others and, when crowned with success, cures the patient more quickly and finally. Indeed, it is difficult to understand why the removal of the overlying cortex and the upper dome of the capsule with consequent fungus formation, as practiced by King (24), Kahn, and others, should be safer

and less damaging than the removal of the abscess intact. Undoubtedly it is possible that a latent inflammatory process may sometimes persist around an abscess and be reactivated even by the most careful handling of the brain tissue. Such a complication, however, may follow any other surgical procedure as well. In fact, this is a frequent consequence of drainage, so much so that Coleman (10) is of the opinion that "this phase of the treatment is still unsatisfactory and that there are inherent risks attending drainage of any kind." Usually, the brain resists such a reactivation of the inflammatory process, having already demonstrated its powers of resistance in limiting and encapsulating the primary focus.

It is certainly true that penicillin, introduced into the abscess cavity through a small burr hole, a very simple procedure, may sometimes sterilize the abscess and consequently cause the capsule to shrink. Yet to leave the capsule *in situ* is equal to leaving in the brain a connective tissue scar which, contracting, must finally cause epilepsy. There is surprisingly little known about this complication of "cured" cerebral abscesses, although one would *à priori* expect epileptic seizures to be a rather frequent sequel of nonradically treated abscesses. Dandy (12), the originator of the method of aspiration of brain abscesses, states that in a few of his patients thus treated epilepsy developed 2 or 3 years later, necessitating the resection of the part or the whole of a cerebral lobe containing the scar of the old abscess. Adson and Craig complain that "epilepsy develops too often following abscess" and that is why they are "gradually becoming convinced that secondary operations, scar resections, as practiced by Penfield, are indicated in selected cases a year or later following the initial operation." Penfield and Erickson (42) noted that 8 patients, out of a group of 33 who recovered from cerebral abscess, have had seizures after operation. In other words, 24 per cent of their patients developed epileptic seizures due to the cicatrix left by the drainage or evacuation of a brain abscess. The patients were all traced for only 1 year or more and the authors presume that "a longer period of follow-up would undoubtedly result in a larger percentage."

Last, but not least, recovery after the radical removal of a brain abscess comes on faster than after its drainage. In the first instance the convalescence lasts weeks, in the second sometimes several months. Finally, it must be emphasized—and this is the result not only of our own observations but also of those of many others—that the enucleation of a brain abscess, although it is large and situated deep in the white matter, damages the brain surprisingly little. In all events, it is by no means more harmful than removal of a large meningioma or other benign brain tumor. The signs and symptoms, which are sometimes many, accompanying brain abscess usually subside completely showing that often the clinical picture is produced chiefly by concomitant brain edema, toxicity of the pus, etc. However, the radical treatment, although theoretically commended by many, was up to now applied only by a few.

Busch advocated the removal of the capsule but only after its incision and the evacuation of the pus, adding that in certain circumstances this procedure is rather simple. Ballance is of the opinion that the treatment of encapsulated cerebral abscesses should consist of their radical removal; he cites however no observations in which this postulate has been realized. Bergmann (6) notes that if during the drainage of an abscess "its membranous wall is forced into the brain incision it should be seized and removed." However, it was Kronlein who first removed a brain abscess *in toto*. He performed this operation on a woman, aged 38 years, who developed jacksonian epilepsy 5 years after a skull injury. At the operation a subcortical abscess, the size of an egg, was found in the left frontal region. The author stresses the fact that such a radical removal of an abscess, which incidentally was diagnosed as brain tumor, presents "a rarity in the literature concerning the subject." Krause states that chronic abscesses should be evacuated and the capsule removed, and Rawling states that since the drainage of an abscess seldom permits a permanent cure, the abscess filling up again as soon as the tube is withdrawn, "it is generally advisable to attempt the entire removal of the abscess wall. As a rule there is no great difficulty attendant

on this process and the haemorrhage is seldom severe." According to Oppenheim (40), Billeter removed a brain abscess *in toto*. Bagley, discussing his 21 cases of cerebral abscess, mentions one in which the lesion was diagnosed as brain tumor and removed radically. The patient recovered, yet the author considers "that we should not be led to practice this method which entails the removal of the protective membrane and exposes the brain to any organisms and may result in a diffuse encephalitis." Sargent has had 5 cases of total removal of posttraumatic cerebral abscess diagnosed properly before the operation. Ballado and Franke, although they are of the opinion that the best treatment of brain abscess is its total removal, assert that this "ideal" is only rarely realized. They say that the capsule of an abscess consists of not one but of several layers which do not represent the true limits of the inflammatory process. Coleman (11) writes that although in rare cases an abscess was successfully removed with its capsule "the danger of encephalitis and the risk of rupture during removal appear too great to allow this to be a premeditated method of dealing with brain abscess." The attitude of the author toward the radical removal of cerebral abscesses is, therefore, negative, in spite of the fact that, as he states, "a recurrence . . . is a possibility in all . . . methods, except perhaps where the entire capsule is removed." In 1946, he apparently changed his opinion as he states that "there is a good deal to be said for the radical extirpation, with the capsule, in multiple abscesses or in those in which a large granulomatous mass forms which cannot be eradicated." Adson and Craig consider that "when it is possible to remove the abscess and capsule without opening it this hastens recovery." Adson, in fact, removed a brain abscess without being aware that he had done so until the mass was opened after operation. The wound healed by primary intention and the patient recovered fully. They say, however, that "our experience with removal of capsule following evacuation of the pus has not been satisfactory, since a secondary suppurative encephalitis develops that is more troublesome to treat than the original infection."

The publication of Clovis Vincent in 1936 was an important milestone on the road leading to the more frequent use of the radical treatment of cerebral abscess (51). His method of dealing with those lesions is as follows: If there is a necessity for surgical intervention in an early stage (only, however, after 3 weeks since the beginning of infection) on account of the severity of the patient's condition, while the abscess is not sufficiently encapsulated to be dealt with radically, it should be localized precisely by means of ventriculography and then the brain decompressed by a large osteoplastic flap, turned down over the site of the lesion. After the aspiration of the pus, the bone flap is replaced without the dura being opened. The aspiration may be repeated. Once the abscess is firmly walled off it is dissected out intact. Applying this method in 3 cases of so-called subacute brain abscess, Vincent obtained complete recovery in all of them. In 2 other cases the abscess was removed *in toto* during the first operation without the brain being decompressed and the abscess aspirated. His assistants, Puech, Thomas, and Brun (45) and Puech, Mahondeau and Askenasy (44) published their own observations of cases in which the abscess was also removed intact. In the second of those 2 cases, the abscess was extirpated from the cerebellum, a unique experience up to that time. Vincent and his coworkers have had, therefore, 6 recoveries in 7 consecutive brain abscesses. In all 7 patients, the lesion was diagnosed properly before the operation and the method of treatment applied with premeditation.

Cairns points out that "in some chronic abscesses the capsule is so thick that the abscess must be removed intact like a tumor, in others the abscess is loculated to such an extent that thorough drainage is impossible and excision is the only treatment. In yet others there are two or three separate though continuous chronic abscesses." Lehman mentions only that radical removal of the brain abscess "is feasible only in cases of old abscesses with a strong capsule and thick contents." Yaskin, Grant, and Groff (56) at a meeting of the Neurological Society in Philadelphia presented 2 cases in which the abscess, diagnosed

as brain tumor, was successfully removed. In the discussion Grant said that he "found it feasible to give the abscess a chance to form and coalesce and then to shell out the whole mass." He thinks that "if the abscess is encapsulated one can do almost anything with it." Dandy's (13) ideas on the subject are different. He states dogmatically that "one would suppose, that because the abscesses undergo a firm encapsulation they are suitable for enucleation with a finger, like some of the brain tumors. Attempts to do so are almost always harmful. The infection which is present in the capsule is still active and it can be easily awakened. A diffuse encephalitis and a wound infection is then unavoidable. I have seen only once an abscess successfully removed." Stich and Bauer believe that "only seldom there is any need for removal of an abscess as in the majority of cases repeated aspirations are sufficient." Odom and Elvidge relate a very interesting experience of complete extracapsular removal of two abscesses, resulting from infection of the brain by the Bacillus typhosus. Northfield strongly advocates enucleation as the proper method in dealing with brain abscesses. In his experience only 1 patient died out of 8 in whom enucleation was carried out. According to him the criteria to guide one as to when to enucleate the abscess are as follows: the subsidence of acute inflammation and the formation of a tough wall. However, if the operation is unduly postponed it becomes technically more difficult owing to the formation of an excessive degree of scarring around the abscess leading to an unnecessarily wide excision of tissue. Secondary loculi or separate, deeply placed abscesses may develop if a case is left too long. The third month, i.e. between 8 and 12 weeks, appears to be the "time of election" for enucleation. Nowicki extirpated radically 8 abscesses of the brain. In 6 cases he obtained good results; in one instance the patient died after the operation from meningitis and in another the patient was taken home soon after the operation in a serious condition and nothing is known about his later fate. Ferens mentions that he removed a brain abscess successfully. Pennybacker reviews the experiences of the Nuffield Department of Surgery in Oxford, and analyses the results of 50 consecutive cases of cerebral abscess. Whereas in the 21 cases in which simple aspiration, tube drainage, open drainage (fungus method), and aspiration plus decompression were performed, there were 13 fatalities; of the 26 cases in which the abscess was enucleated only 2 patients died. Primary extirpation was carried out in 7 cases, extirpation after aspirations in 11, extirpation after aspirations and decompression in 8 cases. One patient who died had multiple bronchogenic abscesses in both hemispheres and the other developed a fatal meningitis after primary extirpation of an abscess due to mastoid infection. In conclusion, Pennybacker states that "we think . . . this method is applicable in most cases and we feel more confident about a lesion dealt with in this manner than in any other because the infective area has been removed from the brain. There is no chronic or quiescent cavity left which may light up in the months or years to come and cause further trouble." Webster, Schneider, and Lofstrom extirpated completely an encapsulated posttraumatic abscess obtaining primary wound healing. Kahn admits that "it is now an accepted fact, that the better encapsulated an abscess, the easier its successful drainage or excision." It seems, however, that actually he does not remove them, even when the abscess has such a thick capsule that its upper pole must be excised before a thorough drainage is instituted.

Sachs, reviewing his experiences with brain abscesses, 6 of which were excised *in toto* and cured, says that no unencapsulated abscess should be drained and that during the acute stage penicillin is an invaluable aid in bringing about encapsulation. Aspiration, except in cerebellar abscesses, should be used only as a palliative procedure until more radical treatment can be instituted. In conclusion he states that "excision without drainage is the ideal procedure" although he adds that "frequently marsupialization must be resorted to if, in the course of an excision, the abscess has been ruptured." According to Fincher, who reports his 5 cases of abscess (1 cerebellar) cured by removal *in toto*, "The results thus far have been such as to suggest that the basic

surgical principle of 'incision and drainage' in the treatment of certain abscesses of the brain might be replaced by total abscess dissection and primary wound closure." Finally, Le Beau advocates the principle of complete extirpation of brain abscess in one stage, whether acute or chronic. With penicillin this is possible, according to him, in most cases without the development of meningitis, even though it may require opening the abscess and often the ventricle. Of his 17 patients, thus treated, 3 died. They were all operated upon before the era of penicillin. Of the 14 patients who were cured, penicillin was used in 13, and in 1 case no penicillin was used. In acute abscesses, that is, before the encapsulation, he turns a flap, opens the dura, and removes not only the abscessed zone but also a large area of contiguous inflammatory and edematous white matter. Thirteen of the 17 abscesses were chronic and 4 were "acute."

The review of the literature shows, so far, that there are on record 52 cases of total removal of brain abscess. In about half of the cases the lesion was diagnosed properly before the operation; in the rest the abscess was taken for brain tumor and excised as such. Of those 52 patients, 8, or at the most 9, died after the operation while all others recovered and in no case did the removal of the abscess reactivate the inflammatory process. It should be re-emphasized that the fear of such a complication represents the main reason why so many who theoretically consider radical treatment as the most rational do not practice it more often.

PERSONAL OBSERVATIONS

Our personal observations deal with 43 cases of cerebral abscesses. In 33 instances the patients were operated upon in the Neurosurgical Service of Neurological Clinic, University of Warsaw, in 4 in the Hospital of the Goodfriars in Cracow, and in 6 in the Neurosurgical Service of the Neurological Clinic, University of Cracow. In 17 patients, the abscess was either drained or tapped and its contents evacuated, and in 26 patients, the lesion was extirpated radically.

Here, we are interested solely with the 26 patients given radical treatment. In 12 of those cases, the abscess was of traumatic origin; in 6, the source of infection was not determined; 5 abscesses were of otogenic origin; in 2 cases, the abscess developed in connection with osteomyelitis of the skull, and in 1 case, most probably, after erysipelas of the face. In 12 cases, the pus contained Staphylococcus aureus nonhemolyticus; in 2, hemolytic staphylococcus; and in 3, nonhemolytic streptococcus. In 9 instances, no bacteriological examination of the pus was carried out due to the very difficult wartime conditions of hospital work. These conditions were the reason no autopsy was done on 1 of the 2 patients who died in the hospital after the operation.

Two patients were operated upon 1 month after the infection; 5, two months after; 6, three months after; 1, ten months after; 4, one year after; and, in 8 patients, the duration of the disease was unknown. More precise data were obtained as to the duration of symptoms from their first appearance to the time of operation: 1 patient was operated upon 2 weeks after it was clear that the injury of the head which he sustained several months previously had produced a brain abscess; 2 patients were operated upon 3 weeks after the onset of the first signs of the disease; 1, four months after; 1, five months after; and 2, twelve months after. In 2 patients, the duration of the symptoms was unknown.

In 8 instances the cerebral abscess, both posttraumatic and resulting from osteomyelitis of the skull, was complicated by an active skin fistula. In 9 cases, the capsule ruptured during the operation; while in 9 cases, it was opened intentionally to facilitate the removal of an abscess of large dimensions. Thirteen patients had an abscess more or less deeply located in the white matter, and in 12 cases, its upper pole was reaching the cortex. In 1 patient, whose case history was lost, the exact location of the lesion is unknown. In 24 patients, the abscess wall was thick, measuring from several millimeters to 1.5 centimeters and more in width; in only 2 instances was the capsule thin, although in 1 patient, the abscess was of 5 weeks', and in another of 8 weeks' duration.

In 6 out of the 26 cases, the abscess was diagnosed before the operation as brain tu-

mor; in the remaining cases, the diagnosis was accurate. One patient has had 3 cerebral abscesses; 4 patients have had 2 abscesses; and in the other patients the lesion was single. In 1 case there was a cerebellar abscess; in the other cases, the abscesses were located in the cerebrum. Two patients were operated upon twice; all others were operated upon only once. One patient left the hospital 16 days after the operation, 1, eighteen days after, and 3, nineteen days after. Eight went home 3 weeks after the enucleation of the abscess, 5, one month, 4, one and a half months, 1, two and a half months, and 1, seventy days after.

Two patients died, 1 of these from meningitis for which he was readmitted to the hospital 2 months after a successful removal of a brain abscess. The meningitis developed acutely after the patient, who felt entirely well, hit a beam with his head. He had been wounded by several fragments of a bomb and only one of these had been removed together with the abscess during the operation. It may be, therefore, that he had a second abscess, unnoticed at the time of operation, which ruptured after the trauma and produced the fatal meningitis. The second patient died 2 weeks after the operation with symptoms of streptococcic meningitis. This patient, whose abscess followed an osteomyelitis of the skull, had had symptoms of meningitis long before the ill-advised operation was performed.

The ultimate fate of 2 patients is unknown although they were feeling well for about 3 years after the operation. Twenty patients recovered fully and were followed up from 2 months to 7 years after the operation. Only 1 patient did not regain the use of his speech, lost because of brain destruction at the time of his injury, although his hemiplegia improved markedly. Another patient has a permanent hemiplegia. Of the followed-up cases, in 1 patient 2 months have elapsed since operation; in 4, three months; in 4, four months; in 1, five months; and in 1, one year. The rest, i.e. 9 patients, were operated upon 1 to 7 years ago. Only 1 of the 9 patients, followed up for more than 1 year after the extirpation of the abscess, is still troubled by epileptic seizures which developed almost immediately after his head injury.

The following observations will illustrate some of the problems which one encounters in dealing with a rather typical, uncomplicated cerebral abscess.

CASE 1. B. M., aged 25 years, was referred to the Neurosurgical Service of the Neurological Clinic, University of Warsaw, on December 29, 1945 (case history No. 1774) by Professor E. Herman of Lodz with a tentative diagnosis of brain abscess. In October 1945, the patient was wounded with a knife in the left parietal region of the skull. After a few days, the skin wound healed completely but the patient noticed loss of sensation in the second finger of his right hand. One month later, he began to suffer from headaches and a fistula discharging a purulent fluid appeared at the site of the previous skin wound. The fistula closed after several days, but the patient began to complain of attacks of numbness in the right half of the lips, the tongue, and in the right hand. Twice the attacks of numbness were followed by loss of consciousness and clonic movements in the right upper extremity Physical examination showed: temperature 36.6 degrees C., pulse 74. In the left parietal region of the skull there was a scar adhering to the bone. The x-ray pictures of the skull showed a small defect in the left parietal bone and, in the middle of it, a foreign body the shape of a broken knife. He had no signs of meningitis but had a hyperemia of both optic discs, especially of the left. There was also an astereognosis and loss of sensation of position and movements of the fingers and of the right wrist. Examination of the blood and the cerebrospinal fluid was essentially negative. With the diagnosis of a cerebral abscess in the left parietal lobe, the patient was operated upon on January 10, 1946. An osteoplastic flap was turned down with the bone defect in its center. During the breaking of the bone flap, the tip of the broken knife was extracted from the scar filling out the bone defect. It was, however, still in the dura which was adherent to the leptomeninges. The blood vessels of the cortex were seen to be cuffed by a white exudate. The swollen brain was incised parallel to the disc made out of the dura and the leptomeninges and after the abscess, the size of a large plum, located just beneath the cortex, had been dissected free from the surrounding softened brain tissue, the whole mass was removed intact. The brain rapidly filled in the cavity resulting from the removal of the abscess. The dura mater was only partially closed because of the tendency of the brain to prolapse. The bone flap was returned to its place and a rubber drain introduced between the oozing bone and the skin. The abscess wall was 1 centimeter thick, the pus dense and greenish. Unfortunately, there was no bacteriological examination of the pus.

The patient withstood the operation well having only a transient paresis of the right upper extremity and a motor aphasia. In the evening, the temperature rose up to 39 degrees C., the following evening descending down to not more than 37.5 degrees C. The fourth day after the operation the sutures were re-

moved and the wound found to be healing by primary intention. However, 3 days later the skin opened in one place and there was a cerebrospinal fistula which closed after 1 week. On February 5, 1946, twenty-five days after operation, the patient left the hospital feeling well. Sixteen months later he is well and working and except for an astereognosis of the right hand has no signs or symptoms of his previous disease.

The patient was operated upon 3 months after the head injury and 8 weeks after the appearance of the first signs of the abscess. Under these circumstances, we felt sure that it would be already well-formed and firmly encapsulated. Our supposition was confirmed. Sixteen months have passed since the operation and we feel, therefore, that we are entitled to presume that the removal of the abscess did not cause an inflammatory process to flare up which might eventually persist in the vicinity of the abscess. In 16 months this would certainly have betrayed itself by some symptoms.

The brain tissue about the abscess was markedly softened, a finding frequently observed in these lesions. However, this is, by no means, an indication of an active inflammation about the abscess. Quite the contrary, "these changes," as pointed out by Penfield (41), "spreading sometimes to both hemispheres may be quite unassociated with encephalitis." The perivascular exudate, seen in the cortex of this, as of many other patients, may be, according to Penfield (41), the only superficial evidence of a brain abscess when it is situated deeply in the brain. The exudate is the expression of the work of macrophages which are discharging, both here and in the white matter, the products of disintegration of the brain tissue.

Neither the blood nor the cerebrospinal fluid of the patient showed any signs of abnormality. This is in agreement with the experiences of many observers in cases of encapsulated cerebral abscesses. Woltman who studied the problem of the changes in the cerebrospinal fluid in cases of brain abscess has come to the conclusion that once the purulent encephalitis is localized and encapsulated, the polymorphonuclears disappear from the fluid and their place is taken by the lymphocytes. "A small number of lymphocytes would seem, on the whole, to indicate better encapsulation, greater resistance and a smoother convalescence after operation. The persistence or reappearance of neutrophiles suggest that encapsulation is not progressing satisfactorily." As is well known, leucocytosis of the blood disappears in later stages of brain abscess either completely or is greatly lowered. A high leucocytic count in the blood suggests rather strongly that the purulent encephalitis has not been fully localized and walled off.

There were also no choked discs, the optic papillae of our patient being only slightly hyperemic. This, too, is in accordance with the experience of others. The presence of a papilledema is not necessary for diagnosis of a brain abscess. On the contrary, a high grade papilledema points to the fact that the encephalitis is still progressing or that the abscess is accompanied by serious swelling of the brain (32). The best time for operation is when the choked discs, if present at all, become stationary, whereas when the papilledema is advancing, the operation is usually dangerous.

CASE 2. H. W., aged 22 years, was admitted to the Neurosurgical Clinic, University of Warsaw, on January 28, 1942 (case history, No. 966). Three weeks previously the patient had been hit with a knife in the left parietal region, at once losing the power in his right extremities. The skin wound healed in 3 days, and 1 week after the injury the paralysis of the right lower extremity began to subside. However, 2 weeks later he complained of headache, nausea and vomiting, and the right lower extremity became once more paralyzed. The physical examination showed: temperature 37.2 degrees C., pulse 50. There was a scar in the left parietal region of the skull but the x-ray pictures of this showed no fracture. The patient had no symptoms of meningitis but a slight papilledema, paresis of the right lower facial nerve, a complete paralysis of the right upper, and a distinct paresis of the right lower extremity were present. There were no sensory changes, no aphasia, and reading, writing, and counting were normal. The blood contained 9,050 white cells. There was little doubt but that the patient was suffering from brain abscess; there was, however, some difficulty in determining its precise location, so that on February 3, 1942, a ventriculogram was made. When attempting to puncture the left lateral ventricle in the occipital region, a resistance was encountered at a depth of about 5 centimeters. After it was forced, some 30 cubic centimeters of semifluid, chocolate-colored, nonodorous matter were aspirated through the exploring needle, and then the cavity was

filled with air. The air was introduced also into the right lateral ventricle. The x-ray pictures revealed, in the left parieto-occipital region of the brain, a cyst measuring 2 by 2.5 centimeters and a dilatation of the right lateral ventricle which was slightly pushed laterally. The bacteriological examination of the contents of the cyst showed nonhemolytic streptococcus. The abscess wall being very thin, there was of course no question of total removal of the lesion. It was decided, therefore, to wait for the firm encapsulation of the abscess and in the meantime, should the condition of the patient call for it, to aspirate it. This was done twice, once on February 17, 1942, and the second time on March 2, 1942. On the first occasion, some 30 cubic centimeters of the same, chocolate-colored matter, containing nonhemolytic streptococci, were evacuated, whereas on the second only a few cubic centimeters of thick, yellow pus, which unfortunately was not examined bacteriologically, were obtained. Between the first and the second puncture of the abscess the leucocytosis in the blood descended to 4,200 cells. The headaches, nausea, and vomiting disappeared, while the paralysis of the right extremities, especially of the arm, was slower to subside.

Finally, on March 12, 1942, nine weeks after the injury and 7 weeks after the appearance of the first signs of the disease, the patient was operated upon. An osteoplastic flap was turned down in the left parieto-occipital region and an abscess, the size of a large walnut, found 3 centimeters beneath the cortex. Its capsule was thick and elastic. The consistency of the brain tissue around the lesion resembled that of an oligodendroglioma. With the aid of the sucker the abscess was dissected free from the brain and the capsule extirpated intact.

The postoperative course was uneventful, although once more there was a complete paralysis of both right extremities. The temperature after the operation was never higher than 38 degrees c. The cerebrospinal fluid examined 24 hours after operation was found to be sterile. On April 3, 1942, that is, 22 days after the abscess had been removed, the patient went home feeling very well subjectively. Objectively, there was complete subsidence of the papilledema and of the paresis of the right lower facial nerve, and the paralysis of the right extremities was distinctly improving. During the first 3 years after operation, the patient felt well and was working. Later we lost track of him.

In spite of the fact that the abscess, situated 3 centimeters beneath the cortex and containing streptococci, was tapped three times and then removed, there was no reactivation of the infection of the brain. The main reason for that is the resistance of the body to the organisms which provoked the original infection.

Since the first symptoms, i.e. paralysis of the extremities, appeared immediately after the head injury, the symptoms of brain abscess following 2 weeks later, it may be presumed that the first sequel of the trauma was an intracerebral hemorrhage which later became infected. This infected hematoma was finally encapsulated so that in the end we were dealing with a brain abscess proper. It is, of course, difficult to see what the method of invasion was in this case. Infection of a thrombus of some of the venae communicantes or a metastasis from a distant source? The skin wound healed 3 days after the injury and there was no osteomyelitis; it may be, therefore, that the infection of hemorrhagic focus came either from a latent otitis or sinusitis, or that it came from some distant source. The fact, however, that the paralysis of the extremities appeared immediately after the injury, as well as the chocolate color of the pus point rather conclusively that the primary lesion was an intracerebral hemorrhage.

As is well known, circumscribed intracerebral hematomas, often diagnosed as brain tumor, are by no means a rarity. Kunicki dealt with them extensively. The gliosis of the brain, found in this case about the abscess, presents another argument for the assumption that the original lesion consisted here in an intracerebral hemorrhage. However, it must be added that instead of softening of the brain tissue around the abscess one may sometimes encounter gliosis and giant cell formation, especially when the abscess is well tolerated. Such changes may sometimes be seen throughout one or even both cerebral hemispheres (41).

When the diagnosis of brain abscess was made, the capsule of the abscess was still very thin, so that it could be tapped only. Had symptoms of intracranial hypertension been more severe, or had they not subsided after the first aspiration, we would have made a decompression followed by repeated aspirations. Yet even if this had contributed to the disappearance of the disease, we would not have been satisfied but would have tried later to excise the capsule. We would have done this from fear that the capsule left *in situ* might provoke epilepsy.

CASE 3. K. S., aged 20 years, was referred to the Neurosurgical Service of the Neurological Clinic,

University of Warsaw, on January 5, 1946, by Dr. K. Kessel from Sochaczew, because of aphasia and jacksonian seizures resulting from a craniocerebral injury sustained 10 days previously. He was hit in the left frontoparietal region of the head by a blunt instrument; he did not lose consciousness and felt quite well for 3 days. Then he had his first seizure of "movements" in the right extremities. In the hospital in Sochaczew he had two similar attacks, recognized as jacksonian seizures. After the second seizure he lost the power in his right upper extremity and he became totally aphasic. For 3 days before admission he had been complaining of frequent vomiting. On admission, the neurological examination showed: temperature 37 degrees C., pulse 56, and in the left frontoparietal region of the head, near the midline, a small longitudinal scar covered by a coagulum of a yellow fluid. X-ray pictures of the skull revealed no fracture. There was a complete motor aphasia, a papilledema on the left, hyperemia of the right optic nerve, a paresis of the right lower facial nerve, some rigidity of the neck, a complete paralysis of the right upper, and a definite paresis of the right lower extremities. The cerebrospinal fluid contained 1.6 per cent of protein and 190 cells, 61 per cent of which were polymorphonuclears and 39 per cent lymphocytes. There was no leucocytosis in the blood. After the admission, the condition of the patient, who was somnolent, confused, and soiling his bed, began to deteriorate. Therefore, it was thought advisable to do a large decompression of the brain, exploring the site of the injury, inasmuch as the possibility of a subdural hematoma could not be excluded. On January 11, 1946, a large osteoplastic flap was turned down over the left frontoparietal region of the brain. The dura mater, which was very tense and did not pulsate, was adherent near the midline to the leptomeninges. The brain was swollen, anemic, and the majority of the cortical blood vessels were cuffed with a white exudate. When the adhesions between the dura mater and the brain were gently ruptured the cortex broke open in one place and began to discharge pus. This was immediately removed by suction and when the whole abscess cavity was apparently empty, almost the whole area of the exposed brain fell in. Since the hole in the cortex, through which the pus was aspirated, was not larger than that which would be left by an exploring brain needle, we confined ourselves to what had already been done, the whole procedure amounting, therefore, to a large decompression of the brain with opening of the dura mater and evacuation of the pus. Bacteriological examination of the pus showed that it contained Staphylococcus albus. The postoperative course was, at first, uneventful and although the patient, who was receiving sulfonamides had a temperature rising to 39 degrees C., his general condition was improving. He gradually improved and ceased to soil his bed. The cerebrospinal fluid, examined a week after operation, contained only 3 cells and 0.165 per cent of protein. However, 8 days after the operation, he had his first bout of high temperature, rigidity of the neck, somnolence, and then, 18 days later, a second bout. Blood examination showed a leucocytosis of 13,950; the cerebrospinal fluid was sterile. We punctured the abscess cavity but found no pus. Unfortunately, the skin incision through which the abscess was tapped would not close and a brain prolapse developed. Coincident with that the paralysis of the right upper, and the paresis of the right lower extremity began to subside and in 2 weeks disappeared completely. Daily dressings and lumbar punctures brought the prolapse to healing, so that on April 13, 1946, that is, 3 months after the operation, the patient could leave the hospital, still aphasic but feeling otherwise entirely well. He had no leucocytosis and the cerebrospinal fluid was normal. Since his operation he has had no epileptic seizures.

He went home without any signs or symptoms, except aphasia, yet he was warned that he might suffer from epilepsy both because of his original brain injury and because the abscess wall had been left *in situ*. He was, of course, advised to take luminal.

For about one month and a half, the patient's condition was very good but then the epileptic seizures reappeared both generalized, and also confined to clonic movements of the right half of the face and the right extremities. The generalized attacks, with loss of consciousness, occurred once a week, whereas the jacksonian seizures, starting always with turning of the eyes to the right, returned more frequently, lately even several times a day. Since the operation, he had been taking 0.1 gram of luminal daily. He was readmitted on October 3, 1946, nine months after the evacuation of the abscess; the neurological examination revealed nothing abnormal, except for motor aphasia which was not improving at all. The examination of the blood and the cerebrospinal fluid was essentially negative.

Assuming that the aggravation of the patient's epilepsy was due to the presence in the brain of the capsule, we decided to excise it. Consequently, on October 10, 1946, the skull was reopened and a brain scar, the size of a large plum, consisting of connective and gliotic tissue, excised. During the excision the left lateral ventricle had to be opened, the cicatrix reaching down to its upper wall. The postoperative course was again, at first, rather stormy, the patient having a temperature over 39 degrees C. His right upper extremity once more became paralyzed and the lower distinctly paretic. The cerebrospinal fluid, examined several times, was found on all occasions to be sterile but containing up to 1,720 white cells (80 per cent polymorphonuclears and 20 per cent lymphocytes) and 3.3 per cent of protein. There was no leucocytosis. This state of affairs lasted for 3 weeks and then definitely improved although the skin incision opened in one place and there was a cerebrospinal fistula which closed only after several days. The paralysis of the right upper and the paresis of the right lower extremity began to subside and the patient felt subjectively well. In spite of the sterility of the cerebrospinal fluid, we thought it safer to treat him with sulfonamides and

penicillin. He received, therefore, some 1,600,000 units of penicillin and a thorough sulfathiazole treatment. On November 16, 1946, six weeks after the excision of the scar, he left the hospital feeling entirely well. He was, of course, aphasic but the power in his right extremities was improving distinctly. He has had a minor attack in his right upper extremity only once during the 7 months which have elapsed since his operation. He was receiving 0.1 gram of luminal, the same amount as before the scar excision.

It is, of course, much too early to say anything about the end-result of scar excision in this patient; there is, however, no doubt that so far since his operation he has had practically no attacks whereas previous to the operation, with the same dose of luminal, they were very severe and occurred daily. Of course, "epilepsy may . . . mar", as pointed out by Pennybacker, "an otherwise good result in cases of brain abscess, however treated, and all of these cases should be kept on regular sedative treatment for several years after operation." Yet, it seems to us that leaving the capsule *in situ* will not improve matters but certainly add to the irritation of the damaged brain.

CASE 4. S.M., aged 20 years, was referred to the Neurosurgical Service of the Neurological Clinic, University of Warsaw, on November 14, 1945 (case history No. 1750) by Dr. J. Kalisz, of Lodz, with a tentative diagnosis of brain abscess. One year previously the patient had had erysipelas of the left half of the head and the face, accompanied by symptoms of general toxemia and meningitis. He remained seriously ill for some weeks and after that complained of headaches localized in the left temporal region. One month ago, his temperature rose, the headache became more severe and he complained of nausea. In the hospital, in Lodz, a bilateral papilledema, signs of meningitis, a motor aphasia and a leucocytosis in the blood and in the cerebrospinal fluid were found. After a thorough treatment with sulfonamides the general condition of the patient improved greatly, yet the choked discs and motor aphasia remained. On admission to the Neurosurgical Service, the patient was confused, had a temperature of 36.8 degrees C., pulse 60, a definite sensitivity of the left temporal region to percussion, a bilateral papilledema, no signs of meningitis, a dilatation of the left pupil, paresis of the right lower facial nerve and of the right upper extremity, and a definite sensory aphasia. The cerebrospinal fluid, containing 0.66 per cent of protein and 26 lymphocytes in 1 millimeter, and showing positive globulin reactions, was sterile. There were 9,750 white cells in the blood. The patient was operated upon on November 23, 1945, with the diagnosis of an abscess in the left temporal lobe. After an osteoplastic flap had been turned down and the dura, strongly adherent to the leptomeninges over the posterior parts of the temporal convolutions incised, an abscess was found some 1.5 centimeters underneath the cortex, the size of an apple; it was easily dissected from the surrounding softened brain tissue. However, during the removal of the abscess its capsule ruptured so that the pus had to be aspirated. Only then was the lesion extirpated. However, there was another abscess, somewhat smaller, beneath the first abscess, and located a little posterior to it. It was removed intact without the capsule being incised. The brain, which had a tendency to prolapse, fell in so that there was no difficulty in closing the dura. The cavity in the brain was filled out with Dakin's solution. The patient who withstood the operation well had an uneventful recovery. For 4 days, he was treated with penicillin given intramuscularly, and 3 days later, he was afebrile. The paresis of the right upper extremity and the motor aphasia subsided 3 days after the removal of the abscess and on December 17, 1945, twenty-four days after operation, he was able to leave the hospital with only a slight paresis of the right lower facial nerve.

Until the middle of April 1946, that is, for 4 months, he felt well; then one day the headache in the left temporal region reappeared and he developed a paresis of the right extremities. The site of the decompression became tense, the skin incision opened in two places and began to discharge a purulent fluid. He was, therefore, readmitted to the Neurosurgical Service on May 9, 1946, (case history No. 1875). The physical examination showed at that time a temperature of 37 degrees C., pulse 68. The patient was psychically clear, without disturbances of speech. The bone flap was somewhat elevated and did not pulsate. There were two small purulent skin fistulas in the line of incision covered by coagulated pus. He had no symptoms of meningitis but had a papilledema, especially on the left, a distinct paresis of the right lower facial nerve and of both right extremities and a hypoesthesia over the right side of the body. The cerebrospinal fluid was sterile. There was no doubt that the patient was suffering from a third brain abscess which had either existed at the time of the previous operation but gone unnoticed, or had been provoked by infection of the operative wound. Since a precise localization of the lesion was difficult, ventriculography was carried out on May 21, 1946, the x-ray pictures of the skull showing definite compression of the anterior horn of the left lateral ventricle. In view of the diagnosis of cerebral abscess in the left frontal lobe, the patient was reoperated upon. The two skin fistulas, underneath which some small bone sequestra were found, were excised and the bone flap raised. The dura was tense and did not pulsate. After it had been opened a large abscess, located anterior to the frontal edge of the skull defect, was found. Its posterior pole was covered by the cortex while the anterior pole was lying outside the frontal lobe, adhering strongly to the dura mater. The ab-

scess, containing some 50 cubic centimeters of thick pus, was with some difficulty dissected free from the dura and finally removed intact. The cavity of the brain was filled out with 10,000 units of penicillin in 10 cubic centimeters of normal saline solution and a rubber drain left for 24 hours. The operation was followed by complete aphasia and an almost complete paralysis of the right extremities. However, the latter subsided after a few days and a week later the patient's speech became normal again. The next day after operation, a second dose of 10,000 units of penicillin was introduced into the abscess bed and on the third postoperative day 10,000 units of penicillin were given intrathecally. One week later, the patient had no temperature and both penicillin, given intramuscularly (25,000 units every 3 hours), and the sulfonamides were stopped. The bacteriological examination of the pus of the third abscess showed the presence of Staphylococcus aureus. The cerebrospinal fluid examined three times during the patient's stay in the hospital was always found to be sterile. On June 6, 1946, nineteen days after the second operation, the patient returned home, feeling well and with no signs or symptoms of his disease. When seen 10 months after the removal of the third abscess he was found to be completely well.

Unfortunately, the pus from the two abscesses removed at the first operation was not examined bacteriologically. We suppose, however, that these two abscesses resulted from infection of the brain by streptococci, which previously caused the erysipelas. The third abscess, extirpated at the second operation, was due to staphylococci which certainly caused the osteomyelitis of the skull also. Both the osteomyelitis and the brain abscess found at the second operation resulted most probably from wound infection at the time of the first operation. In all events, the third abscess, containing staphylococci, could not be a result of erysipelas produced by streptococci. Case 3 of Vincent, David, and Askenasy (53) is somewhat similar to our Case 4, inasmuch as they too found two abscesses in their patient at the first operation, while at the second, performed sometime later, they encountered a third abscess. Their third abscess also resulted from infection but whereas in our patient the infection came most probably from outside, in their case the recurrence of the abscess was due to the fact that they left a portion of the capsule of one of the abscesses at the first operation. The thickness of the wall of their third abscess was almost the same as that of one of the two removed 3½ months previously. They believe, therefore, that the thickness of an abscess wall depends more on the individual reaction of the body to the pathogenic organisms than on the duration of the disease. We agree with that, but with this reservation, that both the duration of the disease and other factors are playing an important rôle in this connection. We agree with them not because our third abscess was as thick as the two removed 6 months previously but on the ground of the observations made in other cases. After all, we do not know that all the three abscesses of our patient did not develop simultaneously. If our assumption that the two first abscesses resulted from the erysipelas is true, then our patient should consider himself lucky, the metastatic abscesses being usually more numerous. In one case of Bergmann (5), of pyemia following gangrene of the bones of the leg, the patient had had 100 cerebral abscesses.

During the removal of one of the first two abscesses the capsule of the abscess ruptured. It is true that the pus was immediately sucked out yet it must be admitted that some of it could have come into contact with the brain. He was treated with penicillin; it is possible, therefore, that the absence of any serious complications in this case as in 8 other cases is to be referred to the action of penicillin, but in 3 other cases in which the capsule was incised during the operation and in which no penicillin was given there was also no infection of the meninges. These last patients were operated on some 3 or 4 years ago and as they are quite well there is no more danger of recurrence of the abscess. The body which has once mastered an infection of the brain, by localizing and encapsulating it, is apparently quite able to resist a new infection by the same organisms. The experiences of Krause, Kahn, and Le Beau who during operations for cerebral abscess several times opened the lateral ventricle without endangering the life of the patient seem to support that view.

According to Hamilton, Whitcomb, and Woodhall, the value of penicillin is highest in the stage of encephalitis which precedes an abscess formation. It helps to localize the inflammatory process. It may also play a great rôle in the treatment of brain abscess by pre-

venting the spread of the infection. Finally, it may sterilize the pus. Since it is almost impossible for penicillin to pass through a capsule the best way to sterilize an abscess is to inject the drug into its cavity. This may be done in doses of 50,000 to 75,000 units once a day or, as was practiced by Shelden, Pudenz, and Craig, doses of 3,000 to 6,000 units given every 3 hours through a small rubber catheter. Besides that the patient receives 20,000 units intramuscularly every 3 hours.

CASE 5. D.A., aged 45 years, was admitted to the Neurosurgical Service of the Neurological Clinic, University of Warsaw, on May 30, 1946 (case history No. 1868). One year previously the patient had been hit in the right frontal region by a fragment of a shell; he lost consciousness for several minutes. After a few days, he was otherwise well but had some headaches and at the site of his injury a fistula, discharging a seropurulent fluid, appeared. Some months ago two small bone sequestra emerged through the fistula. For 1 month, the headaches became very intense and he complained of nausea and vomiting. Physical examination showed a temperature of 36.7 degrees C., pulse 68. In the right frontal region, some 4 centimeters above the superior ridge of the orbita and almost at the midline, a fistula, discharging pus, was found. X-ray films of the skull revealed a defect here, measuring 1 by 0.5 centimeter. The patient showed no signs of meningitis but there was a choked disc on the right, a slight paresis of the left lower facial nerve, a sterile cerebrospinal fluid containing 0.66 per cent of protein and showing positive globulin reactions. There was a leucocytosis.

The patient was operated upon, with the diagnosis of a brain abscess in the right frontal lobe, on June 7, 1946. The edges of the fistula, which were adherent to the borders of the bone defect and to the dura, were excised, the bone defect enlarged to a size of 6 by 6 centimeters, and the dura opened parallel to the edges of the bone defect. Immediately underneath and adhering to it, an abscess the size of a large apple, adhering at the midline to the falx cerebri but otherwise surrounded by softened brain tissue, was encountered. Because of the size of the abscess, it was difficult to extirpate it intact; therefore its capsule was incised and the pus sucked out. The adhesions to the falx were gently ruptured and the capsule dissected free from the brain. The cavity in the brain was filled out with 10,000 units of penicillin in 10 cubic centimeters of normal saline solution and a rubber drain left between the skin and the highly vascularized bone flap. Bacteriologically, the pus contained Staphylococcus aureus. The next day after operation the temperature was between 37 and 38.2 degrees C., there was a slight rigidity of the neck and some headache. The drain was removed after 24 hours and another 10,000 units of penicillin injected into the abscess bed. Two days later the cerebrospinal fluid was withdrawn for bacteriological examination and 10,000 units of penicillin given intrathecally. The fluid was found to be sterile. The temperature, rising up to 38.9 degrees C., continued for a few days and the patient complained of headache and rigidity of the neck. However, a week later he was well and without temperature, so that both the penicillin and the sulfonamides were stopped. On June 23, 1946, sixteen days after operation, he went home without any neurological findings. When last seen, 8 months later, he was found to be entirely well.

Even an active skin fistula is not necessarily a contraindication to removal of an abscess. However, in these cases, the brain should be exposed as little as possible, that is, only by enlarging the already existing bone defect to a size necessary for removal of the capsule. The pus should be previously aspirated. Of the 7 patients who had such a complication of the cerebral abscess, 5 recovered; and in the 2 who died, the infection of the brain and the meninges was not a result of operation.

The patient was operated upon 1 year ago, so we cannot be sure whether he is completely safe from a recurrence of the abscess. However, we have here an additional proof that total removal of an abscess, complicated by a purulent skin fistula, is not necessarily always followed by an encephalomeningitis.

CASE 6. W.U., aged 27 years, was admitted to the Neurosurgical Service of the Neurological Clinic, University of Warsaw, on December 3, 1946 (case history No. 2105). She gave the following history. In September 1944, she was wounded in the right parietal region of the skull by a piece of shrapnel. She immediately lost consciousness and her left extremities became paralyzed. For the next 7 months the wound discharged a purulent fluid. Six months after the injury she developed epilepsy consisting of attacks of loss of consciousness and clonic movements in the left side of the face and left upper extremity. In September 1946, she was operated upon because of her epileptic seizures: some superficial operation was performed. In spite of that and of the treatment with luminal (0.2 gm. daily) she continued to have seizures which had lately become more frequent. Since November 1946, she had had bouts of temperature rising to 39 degrees C., complained of headaches, nausea, vomiting, and loss of memory.

On admission, the patient, who had a temperature of 39 degrees C., a bilateral papilledema, a left hemiparesis with the sign of Babinski, a bone defect in the right parietal bone, measuring 3 by 4 centimeters, covered by an unhealthy skin with a purulent fistula, was co-operative. There were no signs of meningitis. Six hours later she became unconscious and there was a marked bradycardia. A diagnosis of brain ab-

scess in the right parietal region of the brain, complicated by encephalitis, was made and the abscess punctured. The 20 cubic centimeters of thick, greenish pus aspirated from it contained Staphylococcus aureus. The condition of the patient next day was only slightly better, she continued to be very markedly stuporous and the heart beat was still very slow. Consequently, the region of the lesion was exposed and the abscess extirpated intact. Its capsule was very thick and partially calcified, the surrounding brain more softened than is usual in these cases. The postoperative course was stormy, the skin closure breaking open and facilitating a huge brain prolapse. For 4 weeks the patient was very excited and confused, and spoke only French. The temperature was 39 degrees C., but there were no signs of meningitis and the cerebrospinal fluid was continually sterile. After receiving about 6,495,000 units of penicillin (20,000 units into the abscess bed, 750,000 units intrathecally and 5,725,000 intramuscularly) and 133 grams of sulfathiazole (by mouth) she was discharged on February 12, 1947, without temperature, headaches, or attacks, etc. She felt subjectively well; her skin incision had closed completely. When seen 3 months later, she continued to be well, free from attacks, with only the left hemiparesis which had developed after the head injury in 1944 remaining.

Here is the case, our only case, in which the brain abscess was removed in the presence of an encephalitic bout. Undoubtedly, the fact that the patient recovered is wholly due to the chemotherapy. What will be the future of this patient? We will have to wait and see, but certainly the removal of a rather large abscess and the dissection of this abscess from the surrounding inflamed brain tissue, did not provoke a fatal meningitis. As mentioned, Le Beau radically attacks even the "acute abscesses" of the brain, that is, he treats surgically the acute stage of the disease. Of 3 patients thus dealt with 2 died and 1 recovered. It will be for the future to decide whether success will crown the surgical treatment of purulent encephalitis but the beginning is certainly interesting and promising. It was 11 years ago when King (25) was wondering whether sucking out septic brain material would not one day be utilized "in certain suitable cases of suppurative encephalitis or phlegmon of the brain in which there is but little tendency to encapsulate."

GENERAL COMMENT AND CONCLUSIONS

In conclusion, the problem of the radical treatment of cerebral abscesses can be summarized as follows. Purulent encephalitis is either mastered by the body which encapsulates the inflammatory focus, or the infection takes the upper hand over the forces of resistance and the encephalitis spreads over one or even both cerebral hemispheres. The second event takes place when the virulence of the organisms is too great for the forces of defense. The surgeon is, unfortunately, unable to influence this battle greatly; on the contrary, all surgical interference at the early stage of the disease was up to now harmful. Maybe the use of penicillin will change matters.

Experimental researches show that the formation of a capsule around the inflammatory focus starts at the end of the first week after the brain has been infected, the capsule becoming mature at the end of the third week of the disease. It then becomes resistant to the exploring needle and only then can one call such a lesion an "abscess." However, the victory of the body over the infection, resulting in abscess formation, is at the end of the third week still too recent and the wall of the abscess is still too thin to allow it to be treated radically, that is, to be removed intact. The best time for this is, according to our experience, the eighth week after the infection.

During the first 3 weeks of the disease all surgical intervention is usually harmful. If one loses a patient during that period the reason is found in the ability of the body to overcome the infection. At this stage of the disease the causative treatment may consist only of the administration of penicillin which facilitates the limitation of the process of inflammation. Between the third and the eighth week a single or, if necessary, repeated aspirations of the pus are sometimes indicated. Such a procedure can even lead to the subsidence of all the symptoms of the disease. Penicillin introduced into the cavity of the abscess arrests, sometimes completely, the growth of the organisms. It can be given in doses of 10,000 to 75,000 units for 24 hours or of 3,000 to 6,000 units every 3 hours through a small indwelling catheter. If after single or repeated aspirations of the abscess the symptoms of intoxication and increased intracranial pressure do not disappear a decompression of the brain through an osteoplastic flap may seem to be indicated.

However, the capsule of an abscess "cured" by aspiration or drainage, when left behind, is apt to produce epileptic seizures some time later. It is in general difficult for us to find the reason why drainage of an abscess should be preferred to its total removal. For we feel, that, on the contrary, when successful, radical treatment of a brain abscess, may it be of otitic, traumatic or metastatic origin, is as safe as drainage and cures the patient more quickly and more completely. Noteworthy also is the almost complete recovery observed in the majority of cases treated radically. This may be due to the fact that most often cerebral abscesses are located within the white matter where they have a tendency to expand the tracts involved rather than produce their actual destruction. After the removal of the abscess the brain edema subsides, the circulation improves and function returns. The radical method of treatment is, of course, not free from failures but neither are any surgical interventions. At all events, neither our own experience nor that of others confirms the fears expressed by some that the act of separation of the capsule from the surrounding brain tissue is dangerous, producing a flare-up of the inflammatory process which may be present even about an encapsulated abscess. No doubt, such a complication is possible and probably does sometimes happen. The body, however, usually takes good care of it, being at this stage of the disease wholly resistant to the pathogenic organisms which produced the initial infection.

We do not fear the consequences of a premeditated opening or of a rupture of the capsule during the radical procedure, although we take great care, of course, not to let the pus be spread over the operative field. Indeed, experience has taught us that even when the pus, containing organisms, comes into contact with the brain this is not necessarily followed by its reinfection, the resistance of the body being already well established. It must also be added that the pus of a chronic abscess is often sterile, or else the virulence of the organisms is diminished. This is said to be the result of encapsulation of the pus. Finally, we are not afraid to extirpate an abscess complicated by an active skin fistula, being persuaded that if the patient has had no widespread encephalomeningitis before the operation his resistance to the organisms maintaining the activity of the fistula is sufficiently proved. On the other hand, it would seem that an infection of the brain and the meninges by organisms other than those which produced the primary lesion, presents a serious complication. Such a complication, however, is not peculiar to surgical intervention for brain abscess. The use of sulfonamides and of penicillin may still more enlarge the indications for radical treatment of cerebral abscess, those two agents being able to remove the chief contraindication to it, which is, namely, a concomitant purulent leptomeningitis. That complication is the main reason why all other methods of treatment are usually of no avail.

Strong and diffuse adhesions between the capsule of the abscess and the dura mater may make the removal *in toto* very difficult. In such a case the best thing to do is to aspirate the abscess, instill penicillin into its cavity, and then, after the infection has been brought to a standstill, excise the capsule as you would a brain scar. In such cases, Le Beau advocates the removal of the capsule in fragments.

As a rule the removal of an abscess is quite an easy procedure, the brain tissue surrounding the abscess being, in our experience, usually softened and the capsule poorly vascularized. The abscess is usually dissected free from the brain with the aid of the sucker and then enucleated gently with the finger. Adhesions between the dura and the leptomeninges and closing up of the subarachnoid spaces about the abscess are provoked by electrocoagulation or painting of the meninges with a 5 per cent tincture of iodine. However, this is rarely necessary as the subarachnoid spaces are usually closed by spontaneous adhesions. This happens not only in cases of an abscess located superficially but also in those in which the lesion is situated deep under the cortex. One should avoid leaving behind, in the cavity of the brain, strips of muscle, fascia, and such tissues facilitating hemostasis. We are also careful to remove all of the necrotic brain tissue which is, of course, an excellent medium for the growth of micro-organisms. Dakin's solution is used throughout the operation in lieu of

normal saline solution. Before closing, we introduce into the cavity in the brain left after the extirpation of the abscess, as a prophylaxis, 10,000 units of penicillin in 10 cubic centimeters of normal saline solution. The same amount is injected here the next day, and the third day after operation, 10,000 units of penicillin are given in 3 cubic centimeters of cerebrospinal fluid intrathecally, on the occasion of the withdrawal of cerebrospinal fluid for bacteriological examination. Penicillin is also injected intramuscularly (25,000 units every 3 hours), especially when the abscess follows a still active inflammatory focus in the middle ear, or in the sinuses, etc. When the temperature falls and shows no tendency to rise for 3 consecutive days, penicillin is discontinued. In our patients, this was usually done a week after operation, so that the average amount of penicillin given to them did not exceed 1,500,000 units. All our patients were also given various sulfonamides, most often cibasol, in doses of 2 grams every 4 hours, for 2 days, then 3 grams every 8 hours, or 5 grams every 12 hours. As a rule, the abscess bed is not drained but when it was necessary we did drain the cavity using strips of a rubber glove, but only for 24 hours. The dura is usually closed completely.

Using this method in 26 cases of cerebral abscesses (including one cerebellar abscess) of various origins, we obtained in 24 cases a more or less complete recovery. Two patients died. The operative mortality in those 26 cases in which the abscess had been radically removed was therefore less than 10 per cent. The comparison of these results with the results obtained by us when using simple aspiration of the pus or drainage of the abscess explains why we are now strong partisans of radical treatment. Of the 9 patients in whom the abscess was aspirated only, 5 were cured and the other 4 patients died. In 5 of these, the aspiration of the pus was made after the brain had been widely exposed, in 4 cases through a small burr hole. Of the 8 cases in which the abscess was drained 6 survived and 2 died. In 4 patients, the drainage was performed after an osteoplastic craniotomy and in 4 through a small opening in the bone. The operative mortality of these 17 patients was, therefore, 35.3 per cent, that is, three times greater than the mortality of the 26 patients treated radically. In both groups of cases the treatment was instituted at almost the same point in the course of the disease.

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CONGENITAL ANOMALIES

I RECALL many years ago visiting the office of the medical director of one of the large insurance companies. Three of the secretaries had obvious congenital anomalies. The inquiry was made whether these young women were employed on account of the kindheartedness of the director and from charitable motives. The answer was "no," that they were the best secretaries he had ever had and that he believed their defects acted as an inspiration to keep them on the job and always to be polite and courteous. He believed their defects were assets—not liabilities. He further stated that if he had to employ another secretary he would be inclined to search for one with a physical defect.

This incident is cited for the purpose of stimulating those who work to help those individuals affected by congenital defects and to suppress the pessimist who wonders whether it is worth while to devote time, money, study and energy to their relief.

It can be stated with conviction that there are not ten but hundreds or even thousands of individuals leading happy and useful lives who were born with congenital anomalies and whose parents were first told that nothing could be done for them only to find on further inquiry that the defects could be cured or at least much improved.

The advance that has been made in the last twenty-five years in treating these conditions is striking. In the first decade of this century the number of patients afflicted with cleft lip and palate who after numerous operations had been performed, presented an unsightly scar on a deformed lip and a mutilated palate with defective speech was enormous. Although today these unfortunate results still take place, the number is steadily decreasing. On the other hand, the number of patients with these defects who after two or three operations present a well formed lip with an inconspicuous scar and a well reconstructed palate that furnishes good function and little or no speech defect is constantly increasing.

Twenty or thirty years ago the cure of a patient with atresia of the bile ducts was unheard of and the recovery of a patient with atresia of the intestine was regarded as a surgical curiosity. Today, although the mortality of these conditions is still unduly high, the number of recoveries is on the increase.

Due to careful study of embryology and symptomatology intestinal obstruction due to the arrest in the rotation of the midgut can be recognized as a clinical entity and suitable and successful measures adopted for its relief. Likewise, some knowledge of embryology is an important factor in the treatment of duplications of the alimentary tract.

Prior to November, 1939, no patient, so far as I know, with esophageal atresia and tracheoesophageal fistula ever recovered. The condition was either unrecognized or the obstetrician and pediatrician alike advised the parents that a fatal termination was inevitable. Since that time many successful operations for this anomaly have been performed. The first patients to recover were subjected to numerous operations with the construction of an anterior thoracic esophagus. As the defect became more frequently recognized and the patients were brought to the hospital earlier and in better condition, the operation of primary anastomosis of the two esophageal segments has supplanted the earlier operation except under rare circumstances. The roughly 60 per cent drop in mortality in congenital diaphragmatic hernia which has taken place in the last fifteen years could not have been achieved without the recognition of the feasibility of performing major surgical operations in the first few days of life and in this condition the necessity of selecting this time. It is important to recognize early the anomalies of the extremities and bony structures usually cared for by the orthopedic surgeon. Although these anomalies seldom are a threat to life, their early recognition frequently simplifies the treatment and makes the end-result more satisfactory. The success of the treatment of cardiovascular defects which has been so striking in recent years has been made possible only by careful planning, thorough knowledge of the anomalies, of the anatomy of the parts and improvement in anesthesia. Although the operations for these conditions are often not undertaken until later childhood, many of the same factors are essential for a successful outcome that are required in the more acute emergencies.

The anomalies of the genitourinary tract are numerous and here again an intimate knowledge of anatomy and embryology is important in the diagnosis as well as in their successful treatment. Such conditions as ectopic ureter, double ureter, hydronephrosis due to obstruction of aberrant vessels, hydrometrocolpos, exstrophy of the bladder, to mention but a few of the defects of these tracts, have all been successfully treated in recent years. However, their successful treatment has been dependent on familiarity with the possibilities, with factors of development, growth and powers of compensatory hypertrophy as well as experience.

I have mentioned here only some of the congenital anomalies which occur and have indicated that over the last twenty-five years or so, much improvement has taken place in their treatment. There is still much to be done in this field which is a far larger one than is generally recognized.

In order to solve any problem and, in this instance, to improve the lot of individuals handicapped by congenital anomalies, thoughtful planning is necessary. Careful training of the surgeon to cope with these conditions is obviously the first step. As Dr. Gallie pointed out in his presidential address to the American College of Surgeons, "The time allotted to the teaching of anatomy to undergraduates is being so reduced that none but a superman could be expected to acquire any practical knowledge of it." The same statement could be justly applied to embryology. Likewise in medical schools where the teaching of the basic sciences or preclinical subjects is sometimes in the hands of professors who have had no clinical training, or indeed, who are not even holders of an M. D. degree, the correlation between their teaching and its clinical application must of necessity be fragmentary. These statements are made not as a criticism of the excellent preclinical teaching but as a suggestion that it obviously needs to be supplemented

and correlated with clinical work. With the multiplicity of subjects taught in the medical school of today probably the only practical way of adopting this plan would be in the postgraduate training period. For the surgeon who is caring for the congenital anomalies, the desirability of better training in anatomy and embryology is particularly obvious.

The common practice in children's hospitals of having the pediatrician make the surgical diagnoses, running the preoperative and postoperative care and calling a surgical consultant for the operation only, is not a good one. This policy makes of the so called surgeon only a surgical technician or craftsman and the patient necessarily suffers.

Many congenital anomalies require major surgical operations in the first few days or hours of life. The surgeon who undertakes these operations should be familiar with the factors of early development of the infant, of his feeding requirements, of possible blood dyscrasias, of the details of the electrolyte and water balance requirements. All these factors are greatly affected by the operative procedure and should be the responsibility of the surgeon and not of a pediatrician, who cannot be familiar with the factors which alter the requirements and are so often very different from what he is used to. These comments are not intended to belittle the merits of the pediatrician but to suggest that he should occupy the more dignified position of consultant in which he can be of great help rather than to have responsibilities placed upon him which he may not be qualified to accept. In an analogous situation in adult surgery, it is pertinent to ask if the surgeon relies on the internist to make his diagnoses and accept the responsibility for the preoperative and postoperative care.

In the next few decades far greater advances in the treatment of congenital anomalies may be anticipated than in the decades just passed. However, this advance can take place only by having the surgical problems of early life handled by surgeons who are permanent members of the surgical staff of the children's hospitals, rather than by occasional visitors for the purpose of performing a single operation. If surgeons take sufficient interest in the surgery of early life to acquire a better training and if they appreciate their opportunities and responsibilities, the advance in the near future can be unpredictably great. To the surgeon who uses the monetary gauge as the only measure of success, this field should not be recommended. If, however, the surgeon is satisfied with an adequate but modest income and gains more happiness out of making advances in lowering the mortality and improving the lot of those afflicted with anomalies, this field of surgery offers great and very gratifying possibilities.

WILLIAM E. LADD.

CONGENITAL ANOMALIES OF THE FEMALE REPRODUCTIVE ORGANS

EVERY gynecologist and obstetrician possesses at least an elementary knowledge of the embryology of the female sex apparatus—the formation of the genital ridge on the anterior or ventral surface of the mesonephros, the appearance of the gonadal anlage, the invagination of the celomic epithelium to form the muellerian ducts, and the later fusion of the lower portions of the two muellerian ducts to form the uterus and most of the vagina, while the upper unfused portions become the tubes. Knowledge of these few simple facts makes it easy to understand the mechanism of most of the congenital anomalies which he may encounter in practice.

Various portions of the apparatus may be lacking completely (aplasia), or they may fail

to develop beyond the most primitive stages (agenesis), there may be a duplication of various segments, or, much more commonly, there may be a partial or complete failure of fusion of the two muellerian canals. There are, of course, other possible anomalies affecting the lowermost portion of the vagina and the external genitalia, these involving chiefly the derivatives of the urogenital sinus, and often, but not invariably, being associated with anomalies of the upper or muellerian segment.

In the study of such genital anomalies, one should always bear in mind that with them one often finds associated congenital anomalies of the urinary tract, such as absence of the kidney, horseshoe kidney, ectopic kidney or duplication of the kidney. Urography, therefore, should be a routine part of the examination of all such patients.

With any of the enumerated anomalies, the sex characters of the woman, as far as her general body development and her psyche are concerned, may be typically feminine. Just why the local quirks in the development of the sex apparatus occur is still unknown. On the other hand, there is another group of cases, numerically smaller, in which anomalies of the sex apparatus are only a part of a more profound genetic disturbance involving those chromosomal factors which give the primary impetus to the development of the organism along male or female lines.

Sex determination dates from the moment of conception, depending upon the particular chromosomal pattern of the male gamete. The resulting zygote, therefore, is dominantly male or female, depending upon its genic balance, according to the well known theory of Goldschmidt. It is easily possible, in some of the lower forms, to disturb and even invert this genetic sex balance, and similar disturbances undoubtedly occur in the human. The earlier in embryological development such extrinsic factors become operative, the more profound the sex changes which result. Thus are brought about the various forms of true hermaphroditism and pseudohermaphroditism.

While the nature of the disturbing factor is unknown in most cases, endocrinopathies of various sorts, such as those associated with certain adrenal cortical tumors, when these develop in fetal or early postnatal life, explain at least one type of pseudohermaphroditism. A similar factor becoming operative at a later phase of development would produce a much less profound sex change, usually some degree or other of virilism.

I have thought it desirable thus to sketch very briefly the factors concerned in congenital anomalies of the female sex apparatus rather than to try to discuss the latter categorically, which would be obviously out of the question in a short communication such as this. While any of the abnormalities above indicated may at times be encountered in practice, the most frequent are probably congenital absence of the vagina and usually with it the uterus, imperforate hymen, the fusion failures of the muellerian ducts, and hermaphroditism, true and false.

The treatment of congenital absence of the vagina, once a rather formidable problem, has become comparatively, one is tempted to say almost ridiculously, simple. The Baldwin operation so popular in a former day made possible the creation of a vaginal canal which, in my own experience at least, was more nearly perfect than that obtainable by any of the simpler modern methods. But it is no longer a justifiable procedure, because of its magnitude and its very real hazard. This is even more true of operations of the Schubert type, in which a portion of the large bowel was utilized.

While even exceedingly simple methods, like the test-tube pressure plan of Frank, are

used by some and while others still lean to various plastic procedures of the Frank-Geist or Graves type, in which external skin grafts are utilized, it is probable that the most satisfactory method in most cases is that of Wharton, either with or without Thiersch grafts of the vaginal tunnel which can usually be so easily dissected out. Even without grafts the results are very satisfactory, but the addition of the Thiersch grafts appears to be an advantage, though it may call for the co-operation of a trained plastic surgeon.

Most of the fusion anomalies of the muellerian duct involve the uterine segment, producing all the well known variations designated by such terms as uterus didelphys, uterus bicornis unicollis, uterus septatus and subseptatus, uterus arcuatus, etc. Some of these have little practical importance, others may give rise to serious clinical problems, to either the gynecologist or the obstetrician. In only a minority of cases does the condition *per se* call for treatment, but the complications to which it gives rise often do, such as the ectopic pregnancy arising in a rudimentary horn, or the obstetrical problem which can be produced in at least some cases of uterus didelphys as a result of blockage of the birth canal by the nonpregnant half of the double uterus.

As regards hermaphroditism and pseudohermaphroditism, it is gratifying to note the advances which have been made in the treatment of these unfortunate individuals. No longer are they looked upon and perhaps even shunned as freaks of nature, but in most such cases it is possible to make the lot of these patients quite tolerable, and allow them to live their lives as useful members of society. True hermaphroditism is very rare; Young's compilation (1937) revealed only 9 genuine cases, with only a small group since then.

The much more common pseudohermaphrodites are designated as male (pseudohermaphroditismus masculinus) or female (pseudohermaphroditismus femininus) according to the testicular or ovarian character of the gonad. This is ordinarily based on biopsy of the latter, usually calling for exploratory laparotomy, although in some cases one or both gonads are more easily accessible to biopsy, since they may be situated in the inguinal canals or in the lateral portion of the external genitalia, the latter especially in the male pseudohermaphrodites with cleft scrotum. All sorts of combinations of either male or female gonads with accessory sex organs of one sex or another may be encountered, and many interesting problems of surgical nature thus encountered.

Only a few cardinal principles can be touched upon here. The first and, in my opinion, the most important is that the male or female sex nature of the gonad plays a relatively unimportant part in deciding the sex to which the patient is, so to speak, to be socially assigned by the surgeon. Almost never should an adult patient be taken out of the sex category in which she has been raised. The psychologic upheaval which would follow such a step would be enormous and possibly tragic. It is important to know that individuals whose only gonads are testes may be typically female from such standpoints as psychology and libido toward men. Furthermore, the local sex apparatus is far more easily conformed to the female type than the male, involving most often the comparatively simple problem of creating an artificial vagina. In many of these cases the clitoris is comparatively small, with a urethral hypospadias, so that it is simply impossible to convert it into a functioning male organ.

In the second place, it should be remembered that the secondary sex abnormalities, including the appearance of the external genitalia, may often be the same whether the

gonads are ovaries or testes. In most male pseudohermaphrodites in which the individuals have lived as women, the testes have been removed, and in 4 or 5 of such cases, including one of my own, typical menopausal vasomotor symptoms have ensued. It is probably better to conserve one or both gonads, for, contrary to popular belief, they probably exert no "contaminating" influence on the life of the patient.

Finally, and of great importance, is the psychological management of such patients, which may spell the difference between their later happiness or unhappiness. They cannot be treated simply as interesting biological and surgical problems, but as unfortunate human beings with a real cross to bear through life, and with sick and tortured minds as well as malformed bodies. Only a physician with real sympathy and understanding in addition to surgical skill and biological knowledge can measure up fully to the particular requirements of patients with this type of problem.

EMIL NOVAK.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE second edition of *Gynecological and Obstetrical Pathology with Clinical and Endocrine Relations*[1] by Emil Novak, like its predecessor, is written with the clarity characteristic of Dr. Novak's other presentations. The graphic fashion in which the subject matter is described makes it a valuable addition to the medical student's reference bookshelf. The numerous practical clinical observations will appeal both to the general practitioner and to the general surgeon. It is an essential text which should be in the laboratory of every gynecologist and pathologist.

The second edition closely follows the format of the first. The text has been revised to include pertinent new developments accrued since the first edition was published in 1938. More than 100 new illustrations have been added, among which are a number of excellent photographs, in color, of gross specimens. Unfortunately, many of the illustrations, notably the photomicrographs, do not compare in sharpness of detail with the descriptions in the accompanying text. Notable innovations have been made in the chapters on endocrinology of the menstrual cycle and in the several chapters on ovarian hormones. Discussions of stromal adenomyosis, mixed mesodermal tumors of the body of the uterus, mesonephroma of the ovary, and hypernephroid carcinoma of the ovary are welcome additions to the second edition. The several pages devoted to diagnostic methods in the chapter on carcinoma of the cervix include a practical and conservative evaluation of the vaginal smear in the diagnosis of cervical carcinoma. Cognizance is taken of the new developments in Rh incompatibilities in erythroblastosis fetalis. The inference that, in some instances, abortion or sterility may be on the basis of an Rh incompatibility is possibly somewhat premature in a textbook intended for student use.

The author has admirably fulfilled his own idea of a book as expressed in the preface. He has refrained from making it exhaustive or encyclopedic; yet it is sufficiently complete to be of practical value to the clinician and pathologist. JOHN HUFFMAN.

IN reviewing the twelfth edition of *Practical Physiological Chemistry*[2] one is impressed with the remarkable advances in the field of physiological chemistry during the ten years which have elapsed since the previous edition.

This book is familiar to most medical men, for many of whom it served as a text in their first course in physiological chemistry and for whom it has since been cherished as a reference for laboratory methods. The improvement in the text, with inclusion of new material, which has been progressive with each succeeding edition, is particularly notable in the twelfth edition. The book has been largely rewritten, the textual material preceding the experiments or methods given in each chapter has been expanded and, wherever possible, it presents a clear authoritative statement of present opinion, which is invaluable to a student trying to gain fundamental concepts in a new field without being confused by controversial points of view.

As in the previous edition, the field of physiological chemistry is covered in thirty-five chapters including a study of carbohydrates, fats, proteins, the various body tissues, digestion, blood, urine, respiratory exchange, energy metabolism, hormones, vitamins and deficiency diseases. A new chapter (Chapter 36) on antibiotics and metabolic antagonists has been added. The chemistry of the penicillins is briefly discussed and two procedures for assay, the paper disk and the serial dilution methods, are given. Brief consideration is given to streptomycin, gramicidin, and tyrocidine. Under metabolic antagonists is considered a group of compounds with structural similarities but capable of exerting antagonistic effects. The growth-inhibiting effect of sulfanilamide on certain bacteria is reversed by para-aminobenzoic acid. The antagonistic actions of analogues of certain amino acids, as ethionine and methionine, β-2-thienylalanine and phenylalanine, and of such vitamins as pyrithiamine and thiamine, glucoascorbic acid and ascorbic acid, dicumarol and vitamin K, are discussed. The chapter is of more than passing interest to the physician who has not had an opportunity to follow the literature in this special field.

Several other chapters deserve special comment. The chapter on blood and lymph includes a discussion of several newer methods for fractionation of plasma proteins, such as electrophoresis, various concentrations of alcohol at low temperatures, and by appropriate salt concentrations. In the chapter on blood analysis, the subject of photometry is presented in a clear, concise manner. This is especially welcome with the adoption in most laboratories of

[1] GYNECOLOGICAL AND OBSTETRICAL PATHOLOGY WITH CLINICAL AND ENDOCRINE RELATIONS. By Emil Novak, A.B., M.D., D.Sc. (Hon. Dublin), F.A.C.S. 2d ed. Philadelphia and London: W. B. Saunders Co., 1947.

[2] PRACTICAL PHYSIOLOGICAL CHEMISTRY. By Philip B. Hawk, Ph.D., Bernard L. Oser, Ph.D., and William H. Summerson, Ph.D. 12th ed. Philadelphia, Toronto: The Blakiston Co., 1947.

the photoelectric colorimeter in place of the visual colorimeter.

The chapters dealing with intermediary metabolism have been enlarged and much improved. Modern views on the chemistry of muscle contraction are very briefly considered and must be read with the section on carbohydrate metabolism to obtain anything like an adequate understanding of the chemical processes involved.

The text is relatively free from misstatements. Those which do occur are quite evident, as for example on page 421, it is stated that "Experimentally, polycythemia may be produced in animals by the use of phenylhydrazine or the use of cobalt salts in the diet." Obviously the reference to phenylhydrazine, if correct, needs further clarification.

In conclusion, this book justly deserves the favorable acceptance accorded former editions to which it unquestionably is superior. The reviewer has found it a text well adapted for use with classes of medical students, and feels it should have a place in the library of the physician. He will find in it a ready reference to many diagnostic methods and a clear presentation of current biochemical opinion. The book is well indexed. It is hoped that greater care will be taken in binding the book to its covers in future printings. Aside from this the workmanship is good, and the illustrations both numerous and well done. CHESTER J. FARMER.

THE book *The Development of Inhalation Anesthesia*[1] by Barbara Duncum presents a careful and detailed history of inhalation anesthesia, beginning with the discoveries of Priestly and Lavoisier, through the trials of Long, Newton, and associates with ether, and of Snow, Simpson, and others with chloroform in an effort to find a perfect inhalation anesthetic and method of administration. The important anesthetic problem of the period (1846–1900) was ether versus chloroform, and the era was characterized by alternating periods in which the popularity of one or the other as an anesthetic agent predominated. The Royal Medical and Chirurgical Society of London appointed a committee to decide the question, and after animal experiments on the physiological actions of ether and chloroform the committee in 1864 reported that they recommended "mixed anesthesia."

The author concerns herself chiefly with the period 1846 to 1900, and expresses the belief that the social, political, and economic conditions prevailing on the Continent, in England, and America greatly affected the evolution of anesthesia. Only in England had this period been relatively uninterrupted by social, political, and economic unrest, and only in England was the development of anesthesia in the hands of specialist anesthetists, such as John Snow. Elsewhere, the surgeon had the final responsibility for the administration of the anesthetic; he usually started the anesthesia himself and then detailed the continuance of this ". . . necessary, but otherwise insignificant task of keeping the patient anesthetized" to a medical student or some specially trained permanent assistant, often one without medical training. Outside of England research into anesthetic problems was, for all practical purposes, only of academic value as there was little co-ordination or co-operation between the investigators and the surgeons whose chief interest was an insensible and relaxed patient. The result was that on the Continent and in America little real advance in anesthesia was made during this period. The author notes, however, that in America after 1896 it was evident that the specialist anesthetist was gaining more importance and had come to stay.

The introduction of the book outlines the development of inhalation anesthesia during the period under discussion, and the body of the book elaborates the introductions almost completely with direct quotations from contemporary literature and original correspondence. Many reproductions of illustrations of anesthetic apparatus add to the interest of the book.

The author is a member of the Nuffield Department of Anesthetics, University of Oxford, and formerly of the Wellcome Historical Medical Museum, London. These institutions are in possession of the literature and letters from which the detailed, chronological quotations which constitute the bulk of the book were taken.

This work represents much research in accumulating the appropriate material to picture meticulously and interestingly the development of inhalation anesthesia during the last half of the 19th century. The fact that the book is not dull but very interesting, despite the great amount of detail included, is a tribute to the author's skillful tying together of contemporary literature and letters into a unified story. WALLACE HOBBIE.

IN the opinion of the reviewer the authors of *Histopathology of the Ear, Nose and Throat*[2] have presented the most valuable text available covering the entire field. The book is beautifully illustrated and direct and practical in its literature, the result of many years of pathological teaching and allied clinical experience.

The sections devoted to comparative anatomy, embryology, and numerous sections of the normal and pathological finding of external, middle ear, cochlea, labyrinth, and petrous bone are superb—a delight to the otologist. Manifestations of metabolic diseases, allergy, and avitaminosis have been amply covered. The physiology and pathology of the nose and accessory sinuses are carefully described with numerous illustrations (some colored) of changes in the lining membrane of the sinuses.

[1] THE DEVELOPMENT OF INHALATION ANESTHESIA; WITH SPECIAL REFERENCE TO THE YEARS 1846–1900. By Barbara M. Duncum. London, New York, Toronto: Oxford University Press, 1947.

[2] HISTOPATHOLOGY OF THE EAR, NOSE AND THROAT. By Andrew A. Eggston, B.S., M.D., and Dorothy Wolff, A.B., M.A., Ph.D. Baltimore: The Williams & Wilkins Co., 1947.

The comparative anatomy and embryology of the pharynx and larynx with numerous colored illustrations are depicted in a manner to command the attention of every laryngologist.

The publishers are to be commended on the excellence of the paper, type, and illustrations. Truly, a magnificent book. HENRY M. GOODYEAR.

THE book *A Manual of Fractures and Dislocations* by Barbara Bartlett Stimson[1] has been written with the primary purpose of serving as a handbook for medical students and general practitioners. All the essential details of fractures and dislocations are discussed in a brief understandable manner without too much theory or argumentation about disputed points. It is well illustrated with 98 line drawings, showing the points discussed in the text.

In order to keep the book in its most simple form, elaborate technique and detailed operative procedures are purposely omitted and justly so as they would only tend to confuse an individual who does not have a background of clinical fracture experience.

A large number of statistical studies are included in the book, compiled from the fracture service of the Presbyterian Hospital of New York City. These figures are very instructive and add materially to the value of the book.

This manual could be most advantageously used by senior medical students and internes during their preparatory training. It would also be an excellent addition to the library of every general practitioner. CARLO SCUDERI.

THE authors of *A Handbook for the Diagnosis of Cancer of the Uterus by the Use of the Vaginal Smears*[2] state that it was prepared for laboratory use. A careful study of their material and their manner of presentation indicates that not only is it superbly prepared from that standpoint, but also that it contains an excellent discussion of the entire problem of vaginal smears. Their straightforward, unbiased appraisal of the value, the errors, and the difficulties of the procedure appeal to the reader. The 203 photomicrographs are so well reproduced that this book might well be termed an atlas. All phases of pertinent cellular differentiation are pictured. The magnification and the sharpness of the reproductions are such that cellular detail can be readily visualized. In addition, the authors have listed the various types of cells observed under individual headings and give the plate and figure numbers that portray all such cell types. This attention to detail and orderliness on the part of the authors not only makes the study by the reader easier, but also suggests that the same type of thinking is embodied in their entire work.

With this handbook and atlas as a guide, an individual or a laboratory interested in adopting the vaginal smear procedure may save considerable time and effort, make more accurate diagnoses, and avoid "many difficulties which one would never have supposed existed from a perusal of the many reports on the subject." JOHN I. BREWER.

THE name Rotunda Hospital, or simply The Rotunda is well known to all obstetricians throughout the world. This unique institution celebrated its two hundredth anniversary this summer in a most elaborate way and I was fortunate enough to have been invited to participate in the scientific part of the celebration. One cannot but be awed by what this old fashioned hospital has accomplished during the past two centuries. This institution has always had two aims, namely to take care of the poor and needy, and to teach doctors and nurses. No one can deny that these two ambitions have been and are still being fulfilled admirably. Numerous American physicians are grateful for the training in obstetrics which they received in the Rotunda.

Since the founding of the Rotunda on March 15, 1745 by Bartholomew Morse, the work was carried on by such well known names in obstetric history as Ould, Clarke, Labatt, Collins, Macan, Smyly, and Tweedy. In recent years glory has been added to the Rotunda hospital by Jellett, Fitzgibbon, Solomons, Davidson, and the present master Falkiner.

Among the great contributions made for the improvement of obstetrics were the fight against puerperal sepsis, the treatment of eclampsia, and most of all the emphasis on conservatism in the practice of midwifery. Not enough recognition has been given the Rotunda hospital for its struggle against puerperal fever, nor to Tweedy for his contributions to the treatment of eclampsia. As the author points out, Tweedy antedated Stroganoff by one year in his emphasis on the essentials of the conservative treatment of eclampsia. In 1896, Tweedy recommended the control of convulsions by morphine, complete starvation with efficient purgation, and the administration of copious fluids. He also approved of the use of stimulants and the removal of blood by venesection when indicated. Prior to the introduction of Tweedy's treatment of eclampsia at the Rotunda, the mortality rate for eclampsia fluctuated between 16 and 30 per cent. During Tweedy's 7 years' mastership the death rate was 8.6 per cent.

The author of *The Rotunda Hospital 1745-1945*[3], O'Donel Browne, has done full justice to the Rotunda, but this was to be expected. He has the Rotunda spirit in his blood for two reasons. He was an assistant master of the Rotunda, and he is married to the daughter of Tweedy, who was one of the most forceful masters of the Rotunda. The book is not only an accurate historical document but also a scientific treatise. It is delightfully easy to read,

[1] A MANUAL OF FRACTURES AND DISLOCATIONS. By Barbara Bartlett Stimson, A.B., M.D., Med., Sc.D., F.A.C.S. Philadelphia: Lea & Febiger, 1947.

[2] A HANDBOOK FOR THE DIAGNOSIS OF CANCER OF THE UTERUS BY THE USE OF THE VAGINAL SMEARS. By Olive Gates, M.D., and Shields Warren, M.D. Baltimore: Williams & Wilkins Co., 1947.

[3] THE ROTUNDA HOSPITAL 1745–1945. By O'Donel T. D. Browne, M.B., M.A., M.A.O. (Univ. Dub.), F.R.C.P.(I.), F.R.C.O.G. Baltimore: Williams & Wilkins Co., 1947.

because of Browne's style of writing, it is printed in large type on excellent paper, and it is abundantly illustrated. I heartily recommend this book to all individuals interested in the history of medicine and hospitals, and to all physicians interested in obstetrics.

J. P. GREENHILL.

IN a monograph of nearly 300 pages the author of *Anatomia quirurgia del nervio facial*[1] reviews the surgical anatomy of the facial nerve very completely.

The major portion of the treatise is taken up with original work and essentially with descriptive anatomy, based on dissections performed on 16 cadavers. In each case the five separate portions of the facial nerve are studied from its origin to its final distribution. An attempt was made to correlate the final pattern of nerve distribution with the subjects' facial type. Strict correlation seems difficult.

[1]ANATOMIA QUIRURGICA DEL NERVIO FACIAL. By Vicente J. Bertola. Cordoba, Argentina: Imprenta de la Universidad, 1947.

The second part of the work consists of a very brief review of parotid tumors (a clinical paper on the subject is projected for later publication) and a description of the operative procedures employed by various authors in the management of these conditions. The author's own technique also is described at length.

The text is accompanied by numerous illustrations of semidiagrammatic type. Those illustrating the dissections performed are relatively small. Those in the section of the monograph dealing with the surgical aspects of the problem are clearer, however.

The introductory foreword is written by Dr. R. Finochietto.

This volume affords a source of reference based on original work of detailed character, as well as a review of the surgical approaches to exploration in this region of human anatomy where final results may be marred by injury to the facial nerve.

HIRAM T. LANGSTON.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

HANDBOOK ON FRACTURES. By Duncan Eve, Jr., M.D., F.A.C.S. In Collaboration with Trimble Sharber, A.B., M.D. St. Louis: The C. V. Mosby Co., 1947.

ULCER; THE PRIMARY CAUSE OF GASTRIC AND DUODENAL ULCER. DIAGNOSIS, MEDICAL AND SURGICAL TREATMENT, PREVENTION. By Donald Cook, B.A., M.D. Chicago: Medical Center Foundation and Fund, 1946.

EMOTIONAL MATURITY; THE DEVELOPMENT AND DYNAMICS OF PERSONALITY. By Leon J. Saul, M.A., M.D. Philadelphia, London, Montreal: J. B. Lippincott Co., 1947.

PRACTICAL OFFICE GYNECOLOGY. By Karl John Karnaky, M.D. Springfield, Illinois: Charles C Thomas, 1947.

ANDREAS VESALIUS BRUXELLENSIS: THE BLOODLETTING LETTER OF 1539; AN ANNOTATED TRANSLATION AND STUDY OF THE EVOLUTION OF VESALIUS'S SCIENTIFIC DEVELOPMENT. By John B. deC. M. Saunders, F.R.C.S. (Ed.), and Charles Donald O'Malley. New York: Henry Schuman.

CONGENITAL MALFORMATIONS; A STUDY OF PARENTAL CHARACTERISTICS WITH SPECIAL REFERENCE TO THE REPRODUCTIVE PROCESS. By Douglas P. Murphy, M.D., F.A.C.S. 2nd ed. Philadelphia, London, Montreal: J. B. Lippincott Co., 1947.

AMERICAN MEDICAL RESEARCH PAST AND PRESENT. By Richard H. Shryock, Ph.D. New York: The Commonwealth Fund, 1947.

THE 1947 YEAR BOOK OF GENERAL SURGERY. Edited by Evarts A. Graham, A.B. M.D. Chicago: The Year Book Publishers, 1947.

THE DOCTOR IN OREGON; A MEDICAL HISTORY. By O. Larsell. Portland, Oregon: Binsford & Mort for the Oregon Historical Society, 1947.

SURGICAL TREATMENT OF THE ABDOMEN. By Frederic W. Bancroft, A.B., M.D., F.A.C.S., and Preston A. Wade, A.B., M.D., F.A.C.S. Philadelphia, London, Montreal: J. B. Lippincott Co., 1947.

TERAPIA ENDOARTERIOSA. By A. M. Dogliotti. Torino, Italy: Edizioni Minerva Medica S. A., 1947.

ULCERS OF THE STOMACH AND DUODENUM; TECHNIQUE OF SURGICAL TREATMENT. By Edmundo Vasconcelos, M.D., F.A.C.S. Sao Paulo, Brazil: Editora Renascenca S. A., 1937.

GYNECOLOGICAL AND OBSTETRICAL UROLOGY. By Houston S. Everett, M.D. Baltimore: The Williams & Wilkins Co., 1947.

ATLAS OF PRACTICAL INCISIONS AND SOME OPERATIVE PROCEDURES. By Oliver C. Cox, M.D. Baltimore: The Williams & Wilkins Co., 1947.

OBSTETRICS AND GYNAECOLOGY; A REVISION COURSE FOR PRACTITIONERS. By C. Scott Russell and J. Chassar Moir. London, New York, Toronto: Oxford University Press, 1947.

HISTOPATHOLOGIC TECHNIC. By R. D. Lillie, A.B., M.D. Philadelphia and Toronto: The Blakiston Co., 1948.

RECENT ADVANCES IN SEX AND REPRODUCTIVE PHYSIOLOGY. 3rd ed. By J. M. Robson, M.D., D.Sc. (Leeds), F.R.S.E. Philadelphia, Toronto: The Blakiston Co., 1947.

CHRONIC STRUCTURAL BACKACHE DUE TO LOW-BACK STRUCTURAL DERANGEMENT. By R. A. Roberts. London: H. K. Lewis & Co., Ltd., 1947.

SEXUAL BEHAVIOR IN THE HUMAN MALE. By Alfred C. Kinsey, Wardell B. Pomeroy, and Clyde E. Martin. Philadelphia and London: W. B. Saunders Co., 1948.

CONGENITAL MALFORMATIONS OF THE HEART. Helen B. Taussig, M.D. New York: The Commonwealth Fund, 1947.

HISTEROSALPINGOGRAFIA Y PERSUFLACION UTEROTUBARICA QUIMOGRAFICA; LA EXPLORACION DEL FACTOR TUBARICO EN EL ESTUDIO DE LA ESTERILIDAD HUMANANA. By Alberto Eduardo Bettinoti. Buenos Aires: Libreria y Editorial "El Ateneo," 1947.

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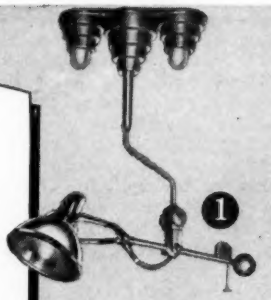

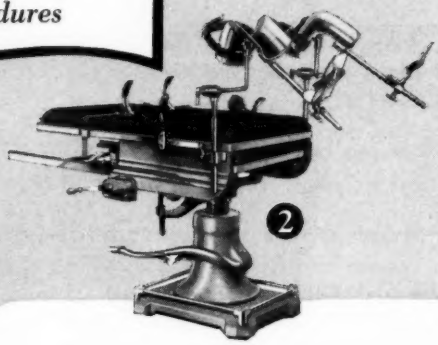

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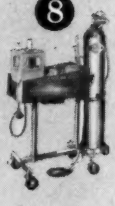

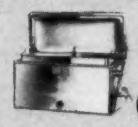

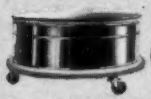

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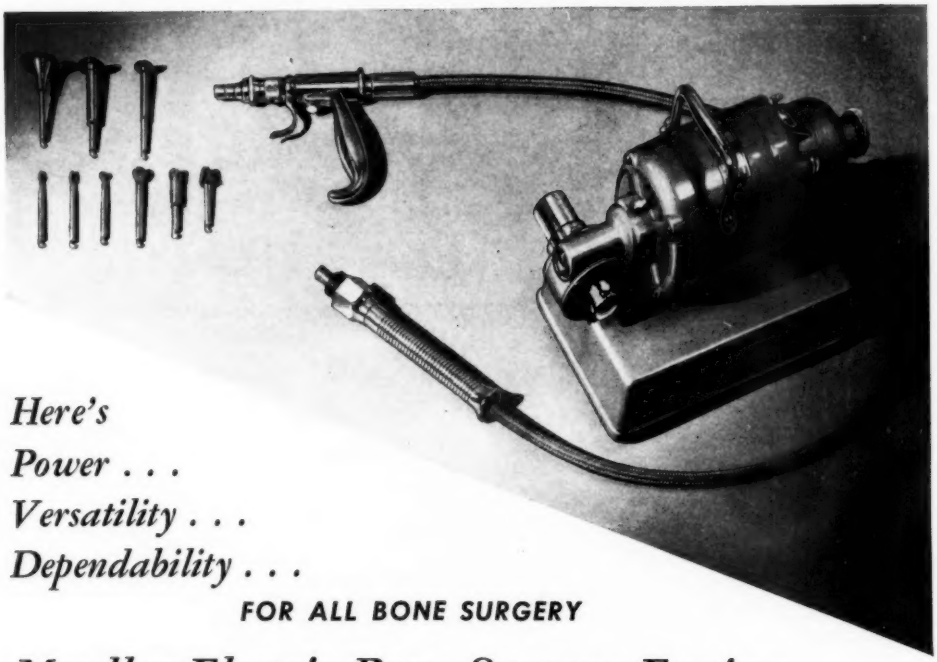

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